



# STIC Search Report

## Biotech-Chem Library

STIC Database Tracking Number: 174388

**TO:** Satayanarayana Gudibande  
**Location:** REM/3C04/3C18  
**Art Unit:** 1654  
**Tuesday, December 20, 2005**

**Case Serial Number:** 10/520791

**From:** Paul Schulwitz  
**Location:** Biotech-Chem Library  
**REM-1A65**  
**Phone:** 571-272-2527

**Paul.schulwitz@uspto.gov**

### Search Notes

Examiner Gudibande,

Please review the attached search results.

If you have any questions or if you would like to refine the search query, please feel free to contact me at any time.

Thank you for using STIC search services!

Paul Schulwitz  
Technical Information Specialist  
REM-1A65  
571-272-2527



(FILE 'HOME' ENTERED AT 09:45:18 ON 20 DEC 2005)

FILE 'LREGISTRY' ENTERED AT 09:49:09 ON 20 DEC 2005

L\*\*\* DEL STRUCTURE

FILE 'REGISTRY' ENTERED AT 09:55:35 ON 20 DEC 2005

L\*\*\* DEL 0 S L\*\*\*

L\*\*\* DEL STRUCTURE

L\*\*\* DEL 0 S L\*\*\*

L\*\*\* DEL STRUCTURE

L\*\*\* DEL 48 S L\*\*\*

D L\*\*\* QUE STAT

D L\*\*\* QUE STAT

L\*\*\* DEL 1052 S L\*\*\* FULL

SAV TEMP L\*\*\* ROYDS420/A

L\*\*\* DEL 0 S L\*\*\* SSS SUB=L\*\*\* SAM

L\*\*\* DEL 1 S L\*\*\* SSS FULL SUB=L\*\*\*

D SCAN

L\*\*\* DEL 603 S L\*\*\* AND NR=3

D QUE STAT L\*\*\*

FILE 'LREGISTRY' ENTERED AT 10:43:41 ON 20 DEC 2005

L1 STRUCTURE

FILE 'REGISTRY' ENTERED AT 10:58:58 ON 20 DEC 2005

L2 0 SEA SSS SAM L1

D L1 QUE STAT

L3 STRUCTURE

L4 0 SEA SSS SAM L3

L5 20 SEA SSS FUL L3

FILE 'HCAPLUS' ENTERED AT 11:03:30 ON 20 DEC 2005

L6 8 SEA ABB=ON PLU=ON L5

FILE 'CAOLD' ENTERED AT 11:03:47 ON 20 DEC 2005

L7 0 SEA ABB=ON PLU=ON L5

FILE 'BEILSTEIN' ENTERED AT 11:04:05 ON 20 DEC 2005

L8 0 SEA SSS SAM L3

L9 2 SEA SSS FUL L3

L10 2 SEA ABB=ON PLU=ON L9 NOT L5

FILE 'MARPAT' ENTERED AT 11:05:22 ON 20 DEC 2005

L11 0 SEA SSS SAM L3

L12 3 SEA SSS FUL L3

L13 0 SEA ABB=ON PLU=ON L12 NOT L6

FILE 'HCAPLUS' ENTERED AT 11:08:12 ON 20 DEC 2005

FILE 'HCAPLUS' ENTERED AT 11:09:19 ON 20 DEC 2005

D QUE STAT L5

FILE HOME

FILE LREGISTRY

LREGISTRY IS A STATIC LEARNING FILE

NEW CAS INFORMATION USE POLICIES, ENTER HELP USAGETERMS FOR DETAILS.

FILE REGISTRY

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 19 DEC 2005 HIGHEST RN 870234-75-6

DICTIONARY FILE UPDATES: 19 DEC 2005 HIGHEST RN 870234-75-6

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH JULY 14, 2005

Please note that search-term pricing does apply when conducting SmartSELECT searches.

\*\*\*\*\*  
\*  
\* The CA roles and document type information have been removed from \*  
\* the IDE default display format and the ED field has been added, \*  
\* effective March 20, 2005. A new display format, IDERL, is now \*  
\* available and contains the CA role and document type information. \*  
\*  
\*\*\*\*\*

Structure search iteration limits have been increased. See HELP SLIMITS for details.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

<http://www.cas.org/ONLINE/UG/regprops.html>

FILE HCAPLUS

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FILE COVERS 1907 - 20 Dec 2005 VOL 143 ISS 26  
FILE LAST UPDATED: 19 Dec 2005 (20051219/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE CAOLD

FILE COVERS 1907-1966

FILE LAST UPDATED: 01 May 1997 (19970501/UP)

This file contains CAS Registry Numbers for easy and accurate substance identification. Title keywords, authors, patent assignees, and patent information, e.g., patent numbers, are now searchable from 1907-1966. TIFF images of CA abstracts printed between 1907-1966 are available in the PAGE display formats.

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file supports REGISTRY for direct browsing and searching of all substance data from the REGISTRY file. Enter HELP FIRST for more information.

FILE BEILSTEIN

FILE LAST UPDATED ON OCTOBER 10, 2005

FILE COVERS 1771 TO 2005.

FILE CONTAINS 9,363,954 SUBSTANCES

>>> PLEASE NOTE: Reaction Data and substance data are stored in separate documents and can not be searched together in one query. Reaction data for BEILSTEIN compounds may be displayed immediately with the display codes PRE (preparations) and REA (reactions). A substance answer set retrieved after the search for a chemical name, a compounds with available reaction information by combining with PRE/FA, REA/FA or more generally with RX/FA. The BEILSTEIN Registry Number (BRN) is the link between a BEILSTEIN compound and belonging reactions. For more detailed reaction searches BRNs can be searched as reaction partner BRNs Reactant BRN (RX.RBRN) or Product BRN (RX.PBRN) .<<<

>>> FOR SEARCHING PREPARATIONS SEE HELP PRE <<<

\*\*\*\*\*

\* PLEASE NOTE THAT THERE ARE NO FORMATS FREE OF COST. \*  
\* SET NOTICE FEATURE: THE COST ESTIMATES CALCULATED FOR SET NOTICE \*  
\* ARE BASED ON THE HIGHEST PRICE CATEGORY. THEREFORE; THESE \*  
\* ESTIMATES MAY NOT REFLECT THE ACTUAL COSTS. \*  
\* FOR PRICE INFORMATION SEE HELP COST \*  
\*\*\*\*\*

NEW

\* PATENT NUMBERS (PN) AND BABS ACCESSION NUMBERS (BABSAN) CAN NOW BE  
SEARCHED, SELECTED AND TRANSFERRED.  
\* NEW DISPLAY FORMATS ALLREF, ALLP AND BABSAN SHOW ALL REFERENCES,  
ALL PATENT REFERENCES, OR ALL BABS ACCESSION NUMBERS FOR A  
COMPOUND AT A GLANCE.

FILE MARPAT

FILE CONTENT: 1988-PRESENT (VOL 143 ISS 24) (20051211/ED)

MOST RECENT CITATIONS FOR PATENTS FROM FIVE MAJOR ISSUING AGENCIES  
(COVERAGE TO THESE DATES IS NOT COMPLETE):

US 6943267 13 SEP 2005  
DE 1020040544 15 SEP 2005  
EP 1577935 21 SEP 2005  
JP 2005272454 06 OCT 2005  
WO 2005097137 20 OCT 2005

Expanded G-group definition display now available.

New CAS Information Use Policies, enter HELP USAGETERMS for details.

MARPATpreviews will be removed from STN on December 31, 2005.

=> file hcplus

FILE 'HCPLUS' ENTERED AT 11:09:55 ON 20 DEC 2005  
 USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.  
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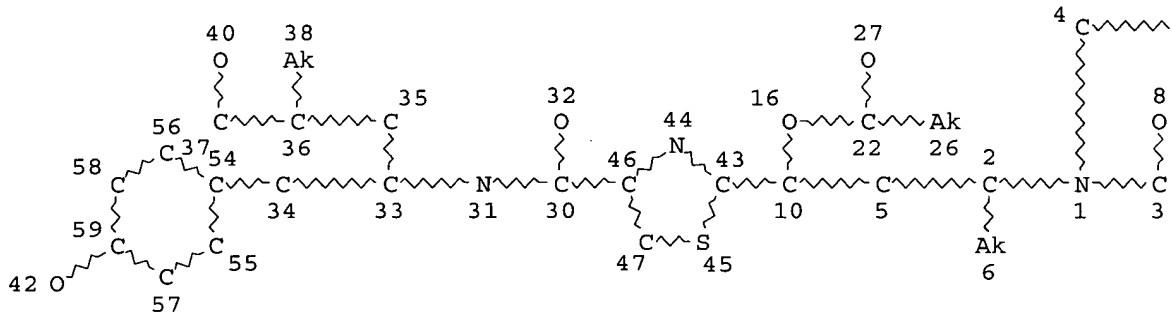
FILE COVERS 1907 - 20 Dec 2005 VOL 143 ISS 26  
 FILE LAST UPDATED: 19 Dec 2005 (20051219/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

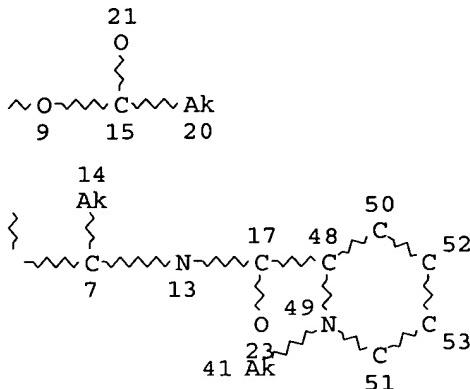
This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d que stat 16

L3 STR



Page 1-A



Page 1-B

NODE ATTRIBUTES:

DEFAULT MLEVEL IS ATOM  
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED  
NUMBER OF NODES IS 50

STEREO ATTRIBUTES: NONE

L5 20 SEA FILE=REGISTRY SSS FUL L3  
L6 8 SEA FILE=HCAPLUS ABB=ON PLU=ON L5

=&gt; d ibib abs hitstr 1-8 16

L6 ANSWER 1 OF 8 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2005:173610 HCAPLUS

DOCUMENT NUMBER: 142:384897

TITLE: Myxobacterial epothilones and tubulysins as promising anticancer agents

AUTHOR(S): Doemling, Alexander; Richter, Wolfgang

CORPORATE SOURCE: R&amp;D Biopharmaceuticals, Muenich, Germany

SOURCE: Molecular Diversity (2005), 9(1-3), 141-147

CODEN: MODIF4; ISSN: 1381-1991

PUBLISHER: Springer

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review. Tubulin-binding agents play a pivotal role in current cancer therapy and there are many efforts in pre-clin. and clin. development of known and novel cytotoxic agents ongoing. In this article a known class, epothilones, as well as a novel class, tubulysins, are presented.

IT 205304-86-5, Tubulysin A

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

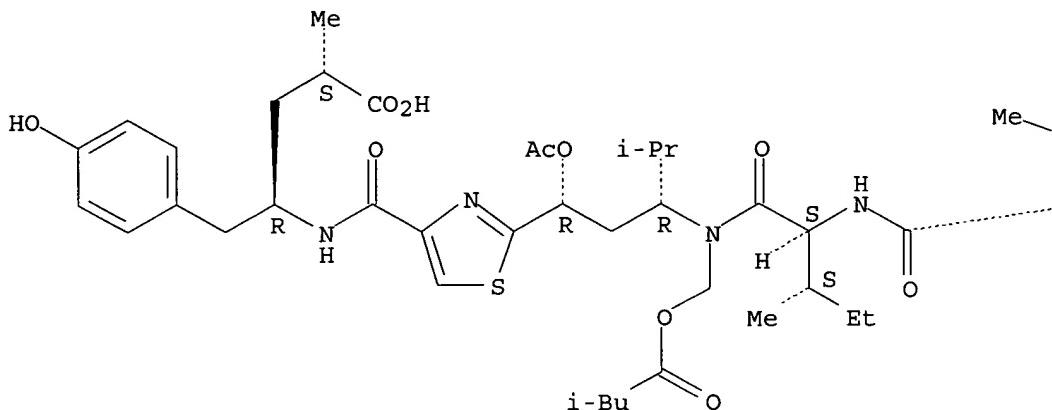
(myxobacterial epothilones and tubulysins as promising anticancer agents)

RN 205304-86-5 HCAPLUS

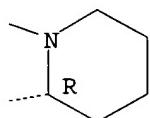
CN Benzenepentanoic acid,  $\gamma$ -[[[2-[(1R,3R)-1-(acetoxy)-4-methyl-3-[(2S,3S)-3-methyl-2-[(2R)-1-methyl-2-piperidinyl]carbonyl]amino]-1-oxopentyl][(3-methyl-1-oxobutoxy)methyl]amino]pentyl]-4-thiazolyl]carbonyl]amino]-4-hydroxy- $\alpha$ -methyl-, ( $\alpha$ S, $\gamma$ R)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 2 OF 8 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:809481 HCAPLUS

DOCUMENT NUMBER: 142:19680

TITLE: Isolation, crystal and solution structure determination, and biosynthesis of tubulysins - powerful inhibitors of tubulin polymerization from Myxobacteria

AUTHOR(S): Steinmetz, Heinrich; Glaser, Nicole; Herdtweck, Eberhardt; Sasse, Florenz; Reichenbach, Hans; Hoefle, Gerhard

CORPORATE SOURCE: Bereich Naturstoffe, Gesellschaft fuer Biotechnologische Forschung mbH, Braunschweig, 38124, Germany

SOURCE: Angewandte Chemie, International Edition (2004), 43(37), 4888-4892, S4888/1-S4888/6

CODEN: ACIEF5; ISSN: 1433-7851

PUBLISHER: Wiley-VCH Verlag GmbH & Co. KGaA

DOCUMENT TYPE: Journal

LANGUAGE: English

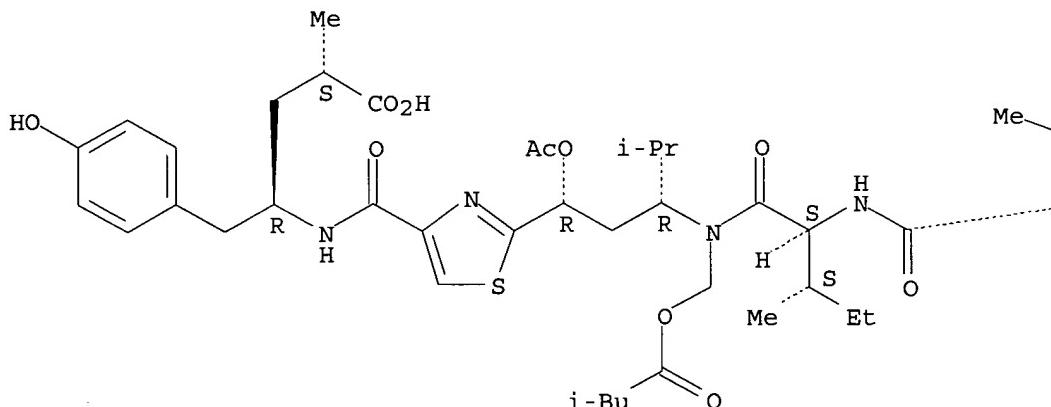
AB Myxobacteria have it both ways: Whereas the epothilones stabilize the

tubulin cytoskeleton and build microtubuli, tubulysins, which have now been isolated from Archangium gephyra and Angiococcus disciformis, have exactly the opposite effect. They induce the disintegration of the microtubuli, and even picomolar concns. can cause cell death by apoptosis. Their effect on cell cultures exceeds that of the most active epothilones by 50-fold.

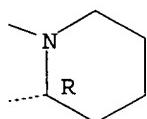
- IT 205304-86-5P, Tubulysin A 205304-87-6P, Tubulysin B  
 205304-88-7P, Tubulysin C 799822-08-5P, Tubulysin G  
 799822-10-9P, Tubulysin I  
 RL: BSU (Biological study, unclassified); PRP (Properties); PUR (Purification or recovery); BIOL (Biological study); PREP (Preparation) (crystal and solution structure determination and biosynthesis of tubulin polymerization-inhibiting tubulysins from Myxobacteria)
- RN 205304-86-5 HCPLUS
- CN Benzenepentanoic acid,  $\gamma$ -[[[2-[(1R,3R)-1-(acetyloxy)-4-methyl-3-[(2S,3S)-3-methyl-2-[[[(2R)-1-methyl-2-piperidinyl]carbonyl]amino]-1-oxopentyl][(3-methyl-1-oxobutoxy)methyl]amino]pentyl]-4-thiazolyl]carbonyl]amino]-4-hydroxy- $\alpha$ -methyl-, ( $\alpha$ S, $\gamma$ R)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

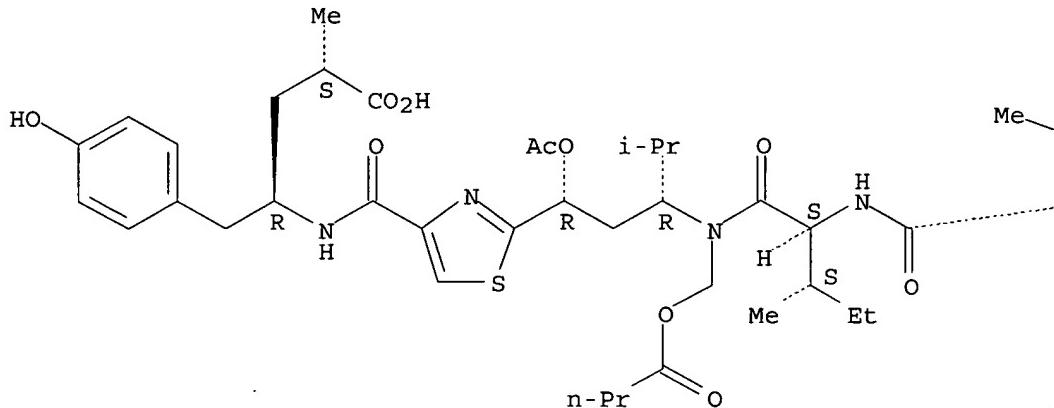


- RN 205304-87-6 HCPLUS
- CN Benzenepentanoic acid,  $\gamma$ -[[[2-[(1R,3R)-1-(acetyloxy)-4-methyl-3-[(2S,3S)-3-methyl-2-[[[(2R)-1-methyl-2-piperidinyl]carbonyl]amino]-1-oxopentyl][(1-oxobutoxy)methyl]amino]pentyl]-4-thiazolyl]carbonyl]amino]-4-

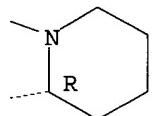
hydroxy- $\alpha$ -methyl-, ( $\alpha S, \gamma R$ ) - (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

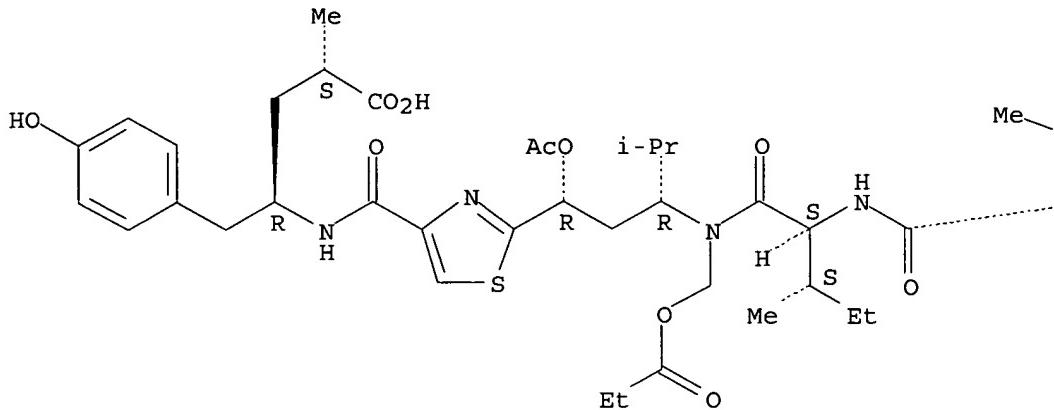


RN 205304-88-7 HCPLUS

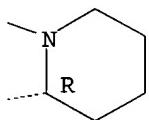
CN Benzenepentanoic acid,  $\gamma$ -[[[2-[(1R,3R)-1-(acetyloxy)-4-methyl-3-[(2S,3S)-3-methyl-2-[[[(2R)-1-methyl-2-piperidinyl]carbonyl]amino]-1-oxopentyl][(1-oxopropoxy)methyl]amino]pentyl]-4-thiazolyl]carbonyl]amino]-4-hydroxy- $\alpha$ -methyl-, ( $\alpha S, \gamma R$ ) - (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

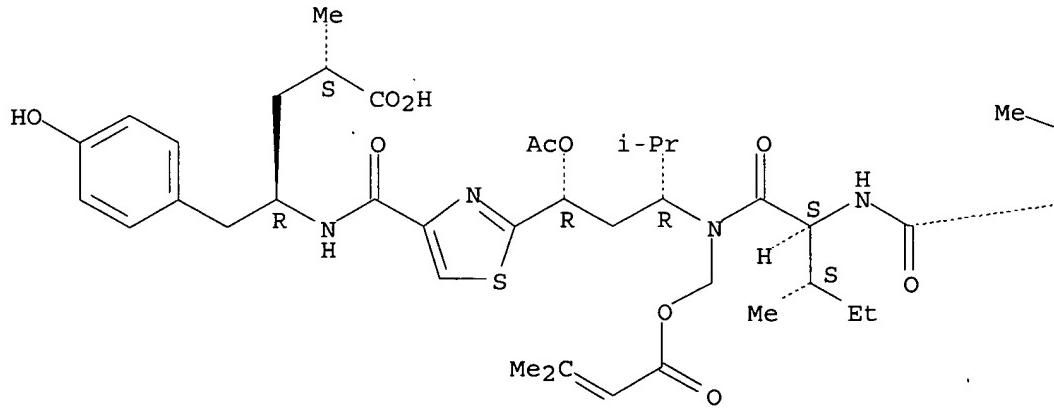


RN 799822-08-5 HCAPLUS

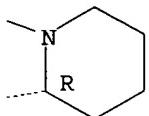
CN Benzenepentanoic acid,  $\gamma$ -[[[2-[(1R,3R)-1-(acetyloxy)-4-methyl-3-[(2S,3S)-3-methyl-2-[[[(2R)-1-methyl-2-piperidinyl]carbonyl]amino]-1-oxopentyl] [[(3-methyl-1-oxo-2-butenyl)oxy]methyl]amino]pentyl]-4-thiazolyl]carbonyl]amino]-4-hydroxy- $\alpha$ -methyl-, ( $\alpha$ S, $\gamma$ R)-  
(9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



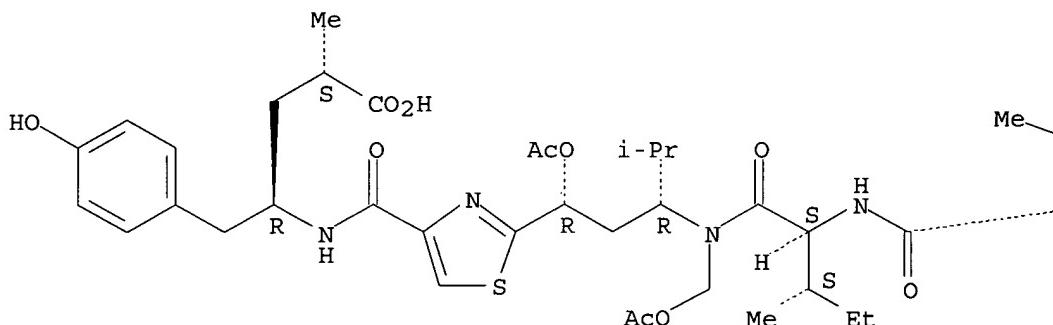
PAGE 1-B



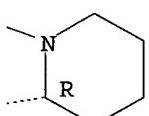
RN 799822-10-9 HCPLUS  
 CN Benzenepentanoic acid,  $\gamma$ -[[[2-[(1R,3R)-1-(acetyloxy)-3-[(acetyloxy)methyl][(2S,3S)-3-methyl-2-[[[(2R)-1-methyl-2-piperidinyl]carbonyl]amino]-1-oxopentyl]amino]-4-methylpentyl]-4-thiazolyl]carbonyl]amino]-4-hydroxy- $\alpha$ -methyl-, ( $\alpha$ S, $\gamma$ R)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 3 OF 8 HCPLUS COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 2004:450512 HCPLUS  
 DOCUMENT NUMBER: 141:23346  
 TITLE: Manufacturing processes for tubulysin derivatives

INVENTOR(S) : Hoefle, Gerhard; Glaser, Nicole; Steinmetz, Heinrich;  
 Leibold, Thomas; Sasse, Florenz  
 PATENT ASSIGNEE(S) : Gesellschaft Fuer Biotechnologische Forschung MbHh  
 (Gbf), Germany  
 SOURCE : Ger. Offen., 34 pp.  
 CODEN: GWXXBX  
 DOCUMENT TYPE: Patent  
 LANGUAGE: German  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 10254439	A1	20040603	DE 2002-10254439	20021121
WO 2004046170	A2	20040603	WO 2003-EP11603	20031020
WO 2004046170	A3	20040701		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG EP 1562979	A2	20050817	EP 2003-775204	20031020
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
PRIORITY APPLN. INFO.:			DE 2002-10254439	A 20021121
			WO 2003-EP11603	W 20031020
OTHER SOURCE(S) :	CASREACT 141:23346; MARPAT 141:23346			
GI				

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB The invention concerns a compound of the subsequent tubulysin general formula I [R = H, C1-4-alkyl, aryl, OR1 NR1R2, NH-(CH2)2-4; R1 = H, C1-6-alkyl, aryl; R2 = H, C1-6-alkyl, aryl; S = H, halo, NO2, NHR3; U = H, halo, NO2, NHR3; R3 = H, HCO, C1-4-alkyl-CO; T = H, OR4; R4 = H, C1-4-alkyl, aryl, COR5, P(O)(OR6)2, SO3R6; R5 = C1-6-alkyl, alkenyl, aryl, heteroaryl; R6 = H, C1-4-alkyl, metal ion; V = H, R7, or (for W = O) O; R7 = H, C1-4-alkyl, COR8; R8 = C1-4-alkyl, alkenyl, aryl; W = H, C1-4-alkyl, (for V = O) O; X = H, C 1-4 alkyl, alkenyl, CH2OR9; R9 = H, C 1-4 alkyl, alkenyl, aryl, COR10; R10 = C1-6-alkyl, alkenyl, aryl, heteroaryl; Y = (for Z = CH3 or COR11) free electron pair or (for Z = CH3) O; R11 = C1-4-alkyl, CF3, aryl and/or Z = (for Y = O or free electron pair) CH3 or (for Y = free electron pair) COR11]. A process for the preparation of I is characterized by the acid-catalyzed splitting of the ester II [R10 = C1-6-alkyl; T = H, OH] (preferably HCl in dioxane) or by a hard base (especially NH3) in alc. (especially MeOH), acylation, reduction, oxidation, alkylation, halogenation, esterification, etherification or reaction with Grignard or alkyllithium reagents. Thus, Tubulysin A benzylamide (III) was prepared from Tubulysin A via amidation of the isobutyryl mixed anhydride with PhCH2NH2 in THF containing EtN(CHMe2)2.

IT 697762-87-1P

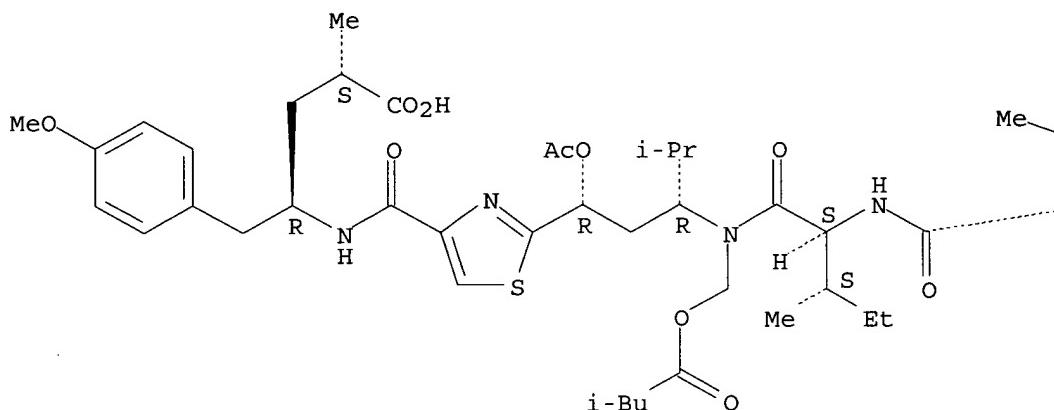
RL: BPN (Biosynthetic preparation); IMF (Industrial manufacture); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (manufacture of tubulysin derivs. via acid or base cleavage of the ester side chain)

RN 697762-87-1 HCAPLUS

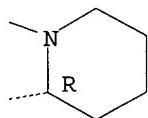
CN Benzenepentanoic acid,  $\gamma$ -[[[2-[(1R,3R)-1-(acetyloxy)-4-methyl-3-[(2S,3S)-3-methyl-2-[[[(2R)-1-methyl-2-piperidinyl]carbonyl]amino]-1-oxopentyl][(3-methyl-1-oxobutoxy)methyl]amino]pentyl]-4-thiazolyl]carbonyl]amino]-4-methoxy- $\alpha$ -methyl-, ( $\alpha$ S, $\gamma$ R)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



IT 697236-83-2P 697236-84-3P 697236-85-4P

697236-86-5P 697751-29-4P, Tubulysin A benzylamide

697751-30-7P, Tubulysin A propyl ester 697762-77-9P

697762-78-0P 697762-79-1P 697762-88-2P

697762-92-8P 698391-61-6P, Tubulysin A methyl ester

698391-62-7P, Tubulysin A propylamide

RL: IMF (Industrial manufacture); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

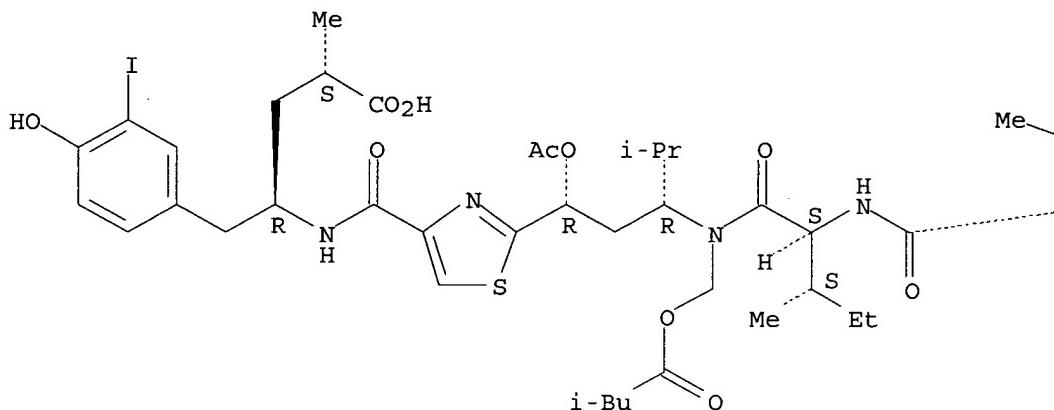
(manufacture of tubulysin derivs. via acid or base cleavage of the ester side chain)

RN 697236-83-2 HCPLUS

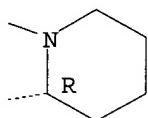
CN Benzenepentanoic acid,  $\gamma$ -[[[2-[(1R,3R)-1-(acetyloxy)-4-methyl-3-[(2S,3S)-3-methyl-2-[[[(2R)-1-methyl-2-piperidinyl]carbonyl]amino]-1-oxopentyl][(3-methyl-1-oxobutoxy)methyl]aminopentyl]-4-thiazolyl]carbonyl]amino]-4-hydroxy-3-iodo- $\alpha$ -methyl-, ( $\alpha$ S, $\gamma$ R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

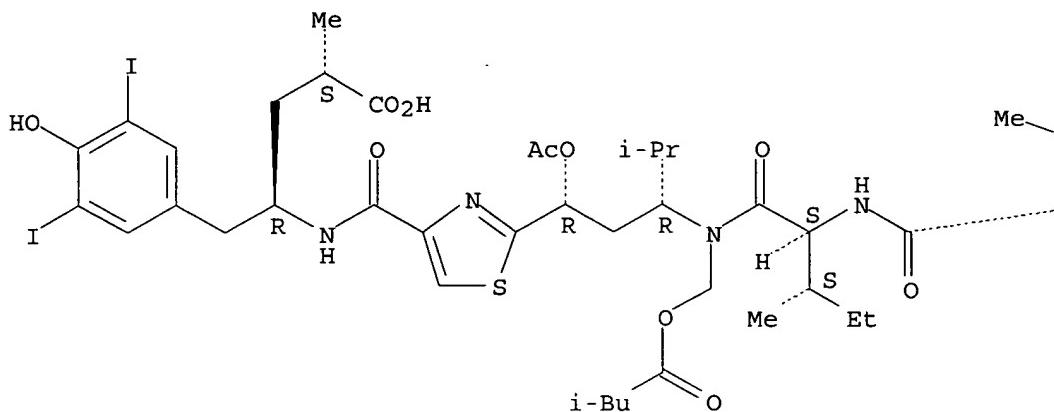


RN 697236-84-3 HCPLUS

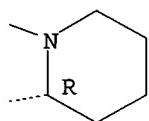
CN Benzenepentanoic acid,  $\gamma$ -[[[2-[(1R,3R)-1-(acetyloxy)-4-methyl-3-[(2S,3S)-3-methyl-2-[[[(2R)-1-methyl-2-piperidinyl]carbonyl]amino]-1-oxopentyl][(3-methyl-1-oxobutoxy)methyl]aminopentyl]-4-thiazolyl]carbonyl]amino]-4-hydroxy-3,5-diido- $\alpha$ -methyl-, ( $\alpha$ S, $\gamma$ R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

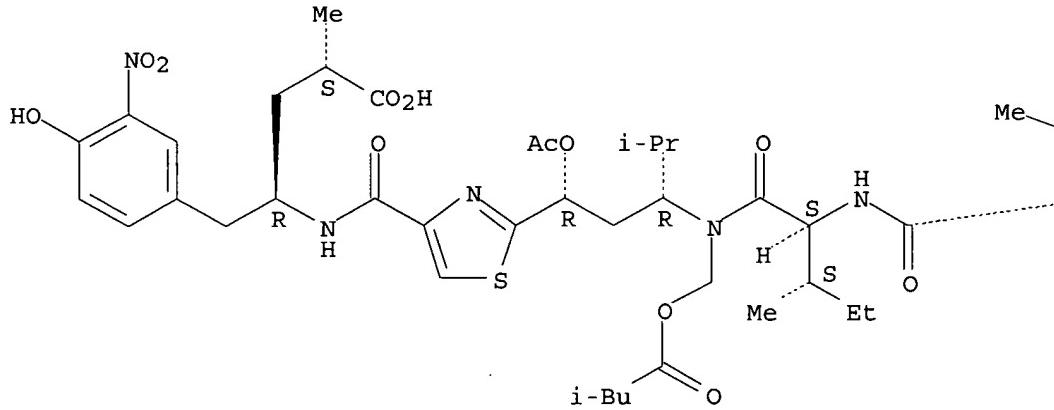


RN 697236-85-4 HCPLUS

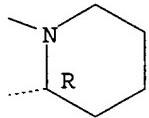
CN Benzenepentanoic acid,  $\gamma$ -[[[2-[(1R,3R)-1-(acetyloxy)-4-methyl-3-[(2S,3S)-3-methyl-2-[(2R)-1-methyl-2-piperidinyl]carbonyl]amino]-1-oxopentyl][(3-methyl-1-oxobutoxy)methyl]amino]pentyl]-4-thiazolyl]carbonyl]amino]-4-hydroxy- $\alpha$ -methyl-3-nitro-, ( $\alpha$ S, $\gamma$ R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

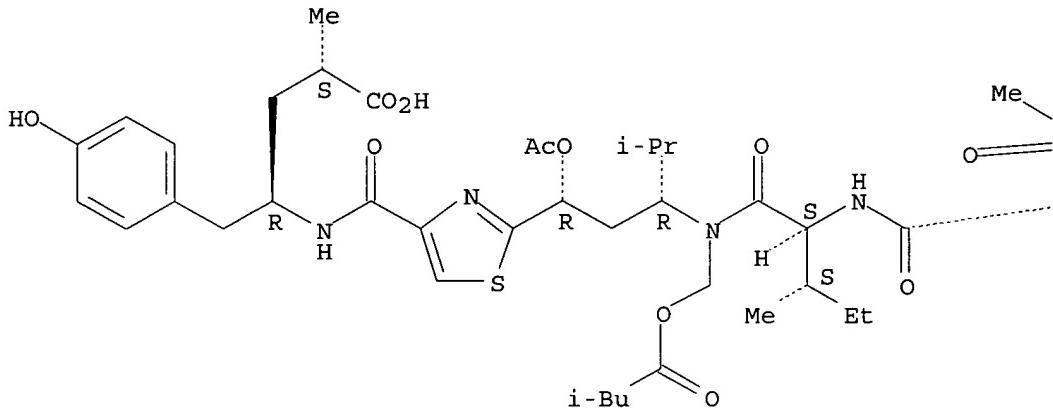


RN 697236-86-5 HCPLUS

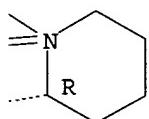
CN Benzenepentanoic acid,  $\gamma$ -[[[2-[(1R,3R)-1-(acetyloxy)-4-methyl-3-[(2S,3S)-3-methyl-2-[[[(2R)-1-methyl-1-oxido-2-piperidinyl]carbonyl]amino]-1-oxopentyl][(3-methyl-1-oxobutoxy)methyl]amino]pentyl]-4-thiazolyl]carbonyl]amino]-4-hydroxy- $\alpha$ -methyl-, ( $\alpha$ S, $\gamma$ R) - (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



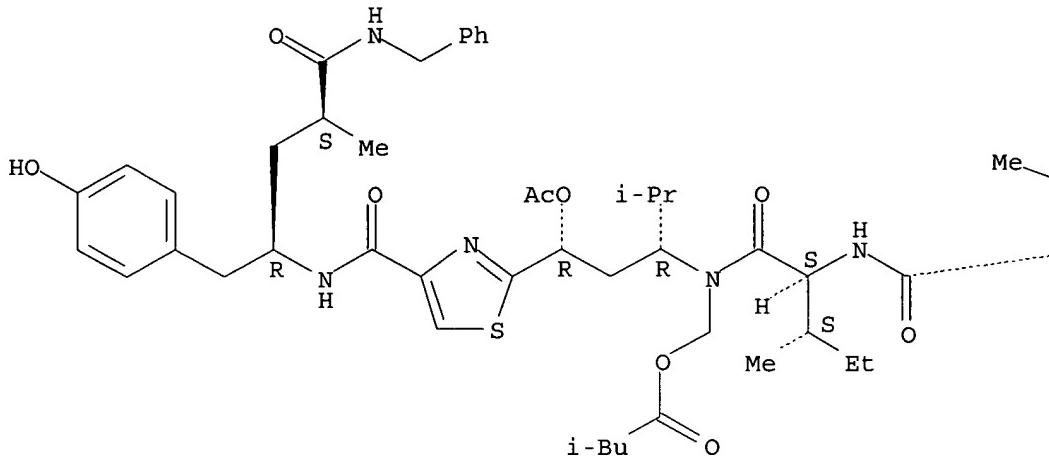
RN 697751-29-4 HCPLUS

CN Butanoic acid, 3-methyl-, [[(1R,3R)-3-(acetyloxy)-3-[4-[[[(1R,3S)-1-[(4-

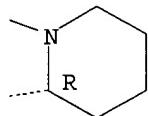
hydroxyphenyl)methyl]-3-methyl-4-oxo-4-[(phenylmethyl)amino]butyl]amino]carbonyl]-2-thiazolyl]-1-(1-methylethyl)propyl][(2S,3S)-3-methyl-2-[[(2R)-1-methyl-2-piperidinyl]carbonyl]amino]-1-oxopentyl]amino]methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

PAGE 1-A



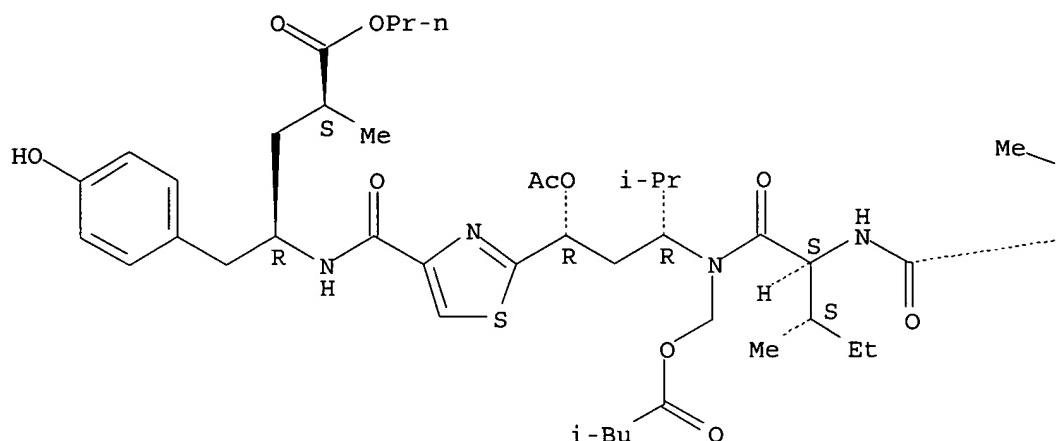
PAGE 1-B



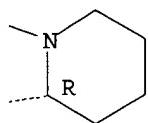
RN 697751-30-7 HCPLUS  
 CN Benzenepentanoic acid,  $\gamma$ -[[[2-[(1R,3R)-1-(acetyloxy)-4-methyl-3-[(2S,3S)-3-methyl-2-[(2R)-1-methyl-2-piperidinyl]carbonyl]amino]-1-oxopentyl][(3-methyl-1-oxobutoxy)methyl]amino]pentyl]-4-thiazolyl]carbonyl]amino]-4-hydroxy- $\alpha$ -methyl-, propyl ester, ( $\alpha$ S, $\gamma$ R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

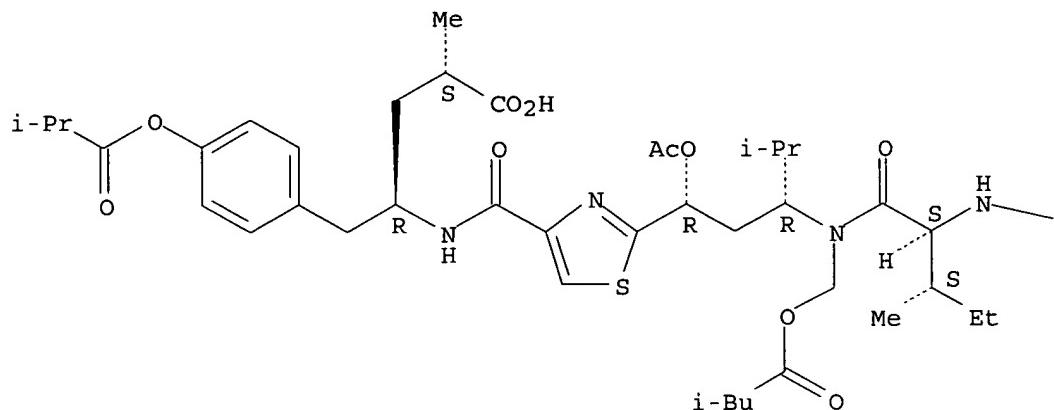


RN 697762-77-9 HCPLUS

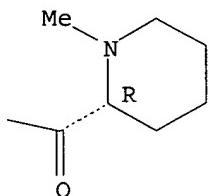
CN Benzenepentanoic acid,  $\gamma$ -[[[2-[(1R,3R)-1-(acetyloxy)-4-methyl-3-[(2S,3S)-3-methyl-2-[[[(2R)-1-methyl-2-piperidinyl]carbonyl]amino]-1-oxopentyl][(3-methyl-1-oxobutoxy)methyl]amino]pentyl]-4-thiazolyl]carbonyl]amino]- $\alpha$ -methyl-4-(2-methyl-1-oxopropoxy)-, ( $\alpha$ S, $\gamma$ R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

PAGE 1-A



PAGE 1-B

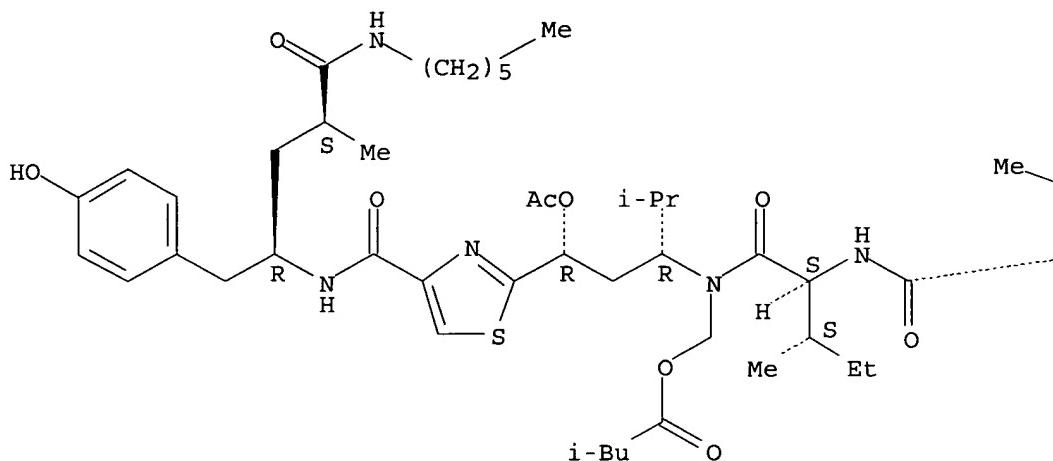


RN 697762-78-0 HCPLUS

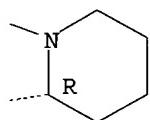
CN Butanoic acid, 3-methyl-, [(1*R*,3*R*)-3-(acetyloxy)-3-[4-[[[[(1*R*,3*S*)-4-(hexylamino)-1-[(4-hydroxyphenyl)methyl]-3-methyl-4-oxobutyl]aminocarbonyl]-2-thiazolyl]-1-(1-methylethyl)propyl][(2*S*,3*S*)-3-methyl-2-[[[(2*R*)-1-methyl-2-piperidinyl]carbonyl]amino]-1-oxopentyl]amino]methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

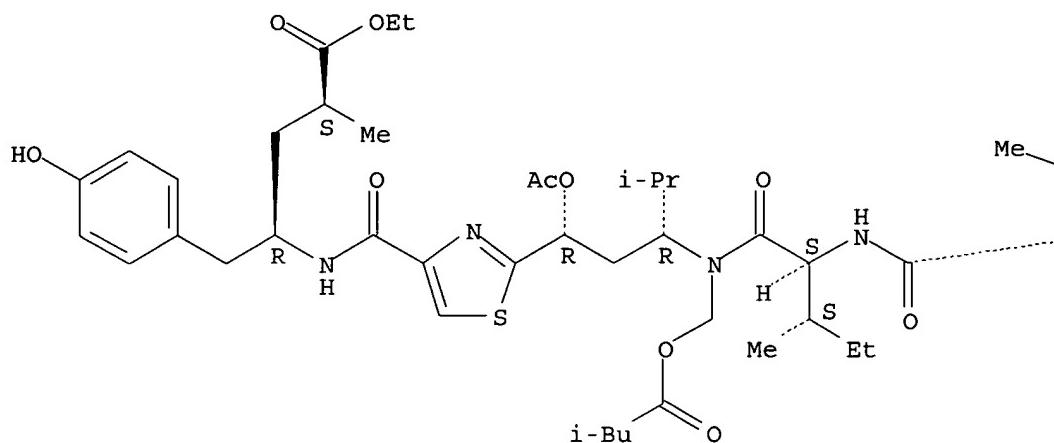


RN 697762-79-1 HCPLUS

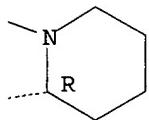
CN Benzenepentanoic acid,  $\gamma$ -[[[2-[(1R,3R)-1-(acetyloxy)-4-methyl-3-oxopentyl]-[(3-methyl-1-oxobutoxy)methyl]amino]pentyl]-4-thiazolyl]amino]-4-hydroxy- $\alpha$ -methyl-, ethyl ester, ( $\alpha$ S, $\gamma$ R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

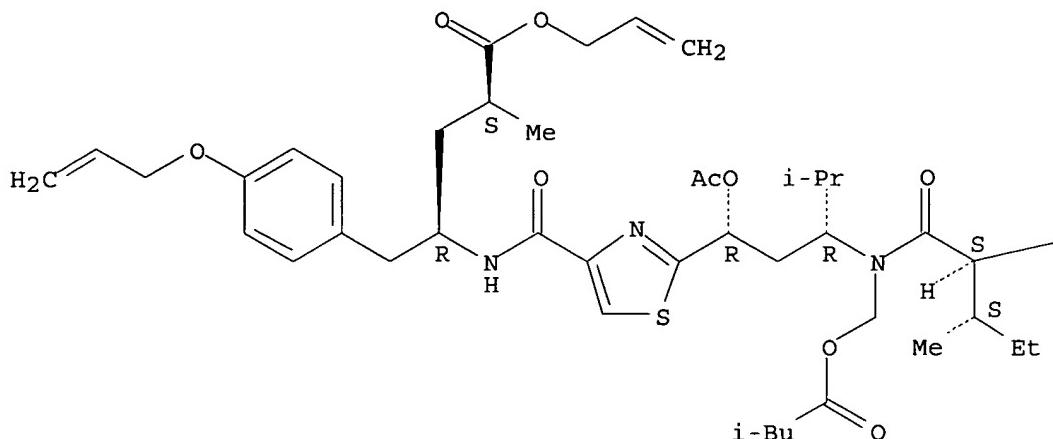


RN 697762-88-2 HCPLUS

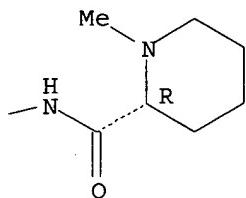
CN Benzenepentanoic acid,  $\gamma$ -[[[2-[(1R,3R)-1-(acetyloxy)-4-methyl-3-[(2S,3S)-3-methyl-2-[[[(2R)-1-methyl-2-piperidinyl]carbonyl]amino]-1-oxopentyl][(3-methyl-1-oxobutoxy)methyl]amino]pentyl]-4-thiazolyl]carbonyl]amino]- $\alpha$ -methyl-4-(2-propenyl)-, 2-propenyl ester, ( $\alpha$ S, $\gamma$ R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



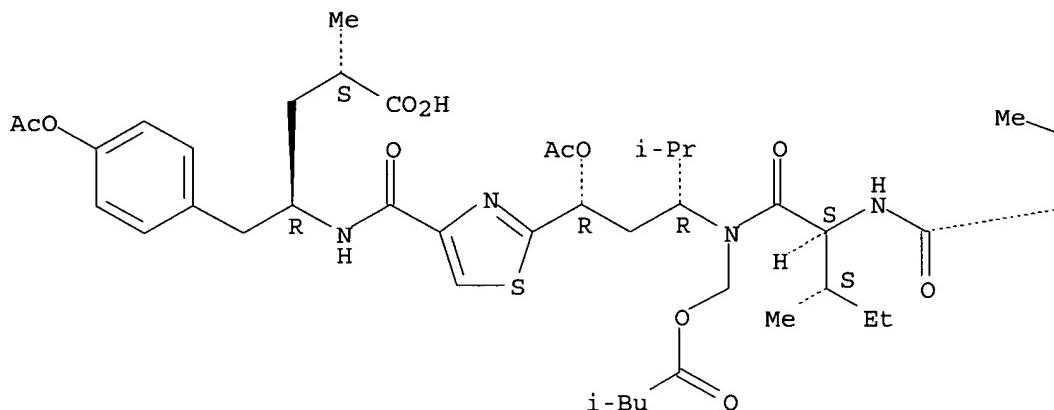
PAGE 1-B



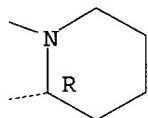
RN 697762-92-8 HCAPLUS  
 CN Benzenepentanoic acid, 4-(acetyloxy)- $\gamma$ -[[[2-[(1R,3R)-1-(acetyloxy)-4-methyl-3-[(2S,3S)-3-methyl-2-[(2R)-1-methyl-2-piperidinyl]carbonyl]amino]-1-oxopentyl][(3-methyl-1-oxobutoxy)methyl]amino]pentyl]-4-thiazolyl]carbonyl]amino]- $\alpha$ -methyl-, ( $\alpha$ S, $\gamma$ R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

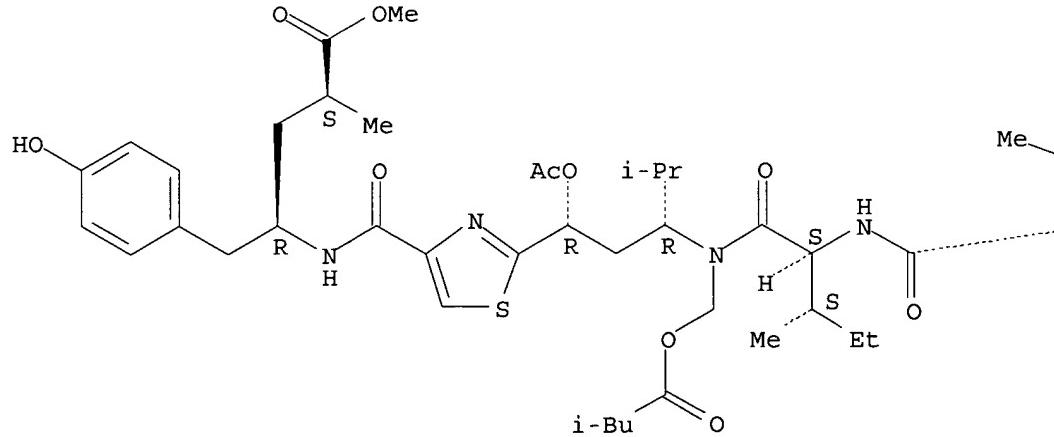


RN 698391-61-6 HCPLUS

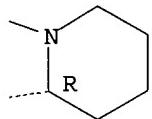
CN Benzenepentanoic acid,  $\gamma$ -[[[2-[(1R,3R)-1-(acetoxy)-4-methyl-3-[(2S,3S)-3-methyl-2-[(2R)-1-methyl-2-piperidinyl]carbonyl]amino]-1-oxopentyl][(3-methyl-1-oxobutoxy)methyl]amino]pentyl]-4-thiazolyl]carbonyl]amino]-4-hydroxy- $\alpha$ -methyl-, methyl ester, ( $\alpha$ S, $\gamma$ R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

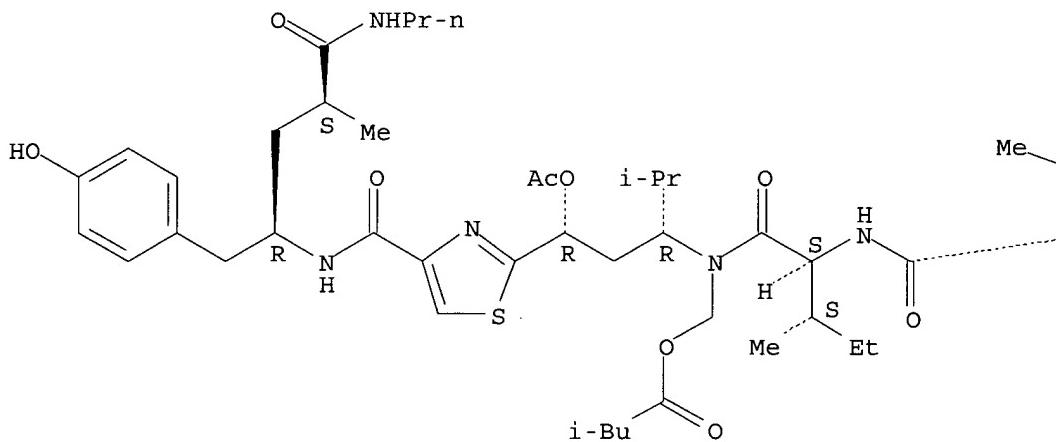


RN 698391-62-7 HCPLUS

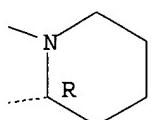
CN Butanoic acid, 3-methyl-, [(1*R*,3*R*)-3-(acetyloxy)-3-[4-[[[(1*R*,3*S*)-1-[(4-hydroxyphenyl)methyl]-3-methyl-4-oxo-4-(propylamino)butyl]amino]carbonyl]-2-thiazolyl]-1-(1-methylethyl)propyl][(2*S*,3*S*)-3-methyl-2-[[[(2*R*)-1-methyl-2-piperidinyl]carbonyl]amino]-1-oxopentyl]amino]methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



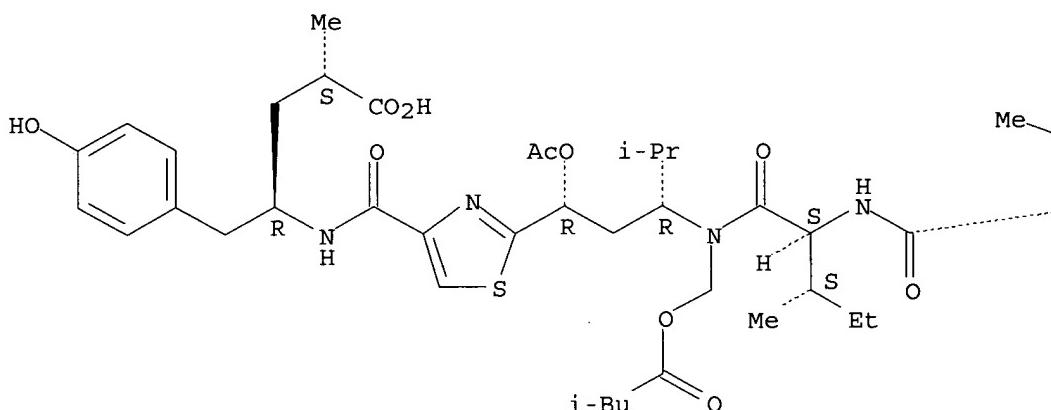
IT 205304-86-5, Tubulysin A 205304-87-6, Tubulysin B  
 205304-88-7, Tubulysin C  
 RL: RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT  
 (Reactant or reagent); USES (Uses)  
 (manufacture of tubulysin derivs. via acid or base cleavage of the ester  
 side chain)

RN 205304-86-5 HCAPLUS

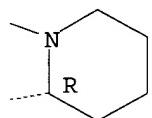
CN Benzenepentanoic acid,  $\gamma$ -[[[2-[(1R,3R)-1-(acetoxy)-4-methyl-3-  
 [(2S,3S)-3-methyl-2-[[[(2R)-1-methyl-2-piperidinyl]carbonyl]amino]-1-  
 oxopentyl][(3-methyl-1-oxobutoxy)methyl]amino]pentyl]-4-  
 thiazolyl]carbonyl]amino]-4-hydroxy- $\alpha$ -methyl-, ( $\alpha$ S, $\gamma$ R)-  
 (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

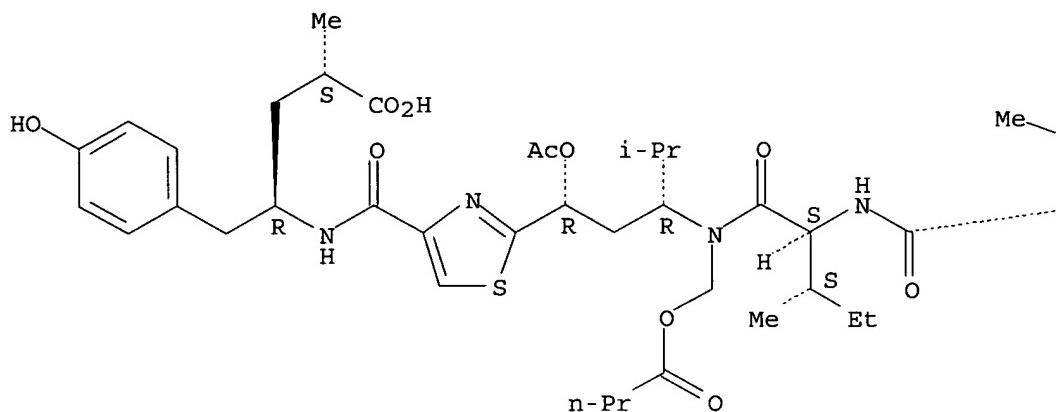


RN 205304-87-6 HCAPLUS

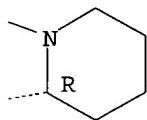
CN Benzenepentanoic acid,  $\gamma$ -[[[2-[(1R,3R)-1-(acetoxy)-4-methyl-3-  
 [(2S,3S)-3-methyl-2-[[[(2R)-1-methyl-2-piperidinyl]carbonyl]amino]-1-  
 oxopentyl][(1-oxobutoxy)methyl]amino]pentyl]-4-thiazolyl]carbonyl]amino]-4-  
 hydroxy- $\alpha$ -methyl-, ( $\alpha$ S, $\gamma$ R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

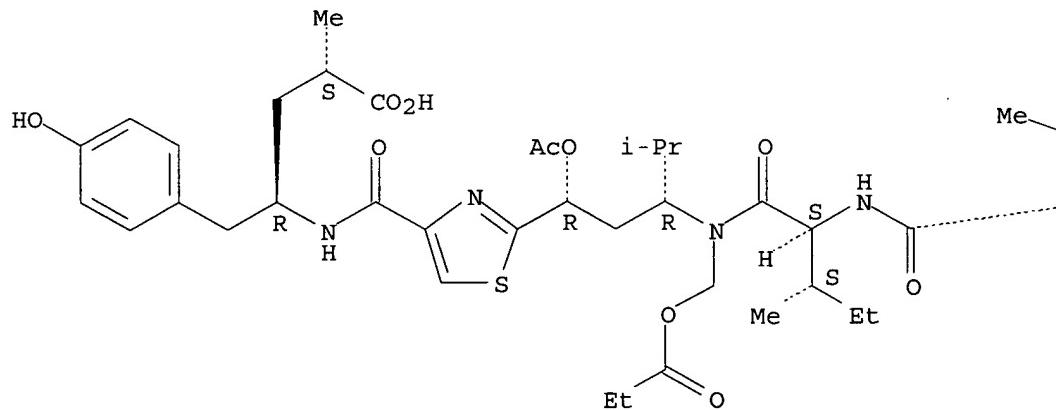


RN 205304-88-7 HCAPLUS

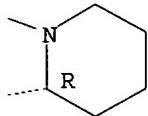
CN Benzenepentanoic acid,  $\gamma$ -[[[2-[(1R,3R)-1-(acetyloxy)-4-methyl-3-[(2S,3S)-3-methyl-2-[([(2R)-1-methyl-2-piperidinyl]carbonyl]amino]-1-oxopentyl][(1-oxopropoxy)methyl]amino]pentyl]-4-thiazolyl]carbonyl]amino]-4-hydroxy- $\alpha$ -methyl-, ( $\alpha$ S, $\gamma$ R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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IT 697236-88-7P, Tubulysin A methyl ether methyl ester  
 RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)  
 (preparation and enzymic hydrolysis of; manufacture of tubulysin derivs.

via acid

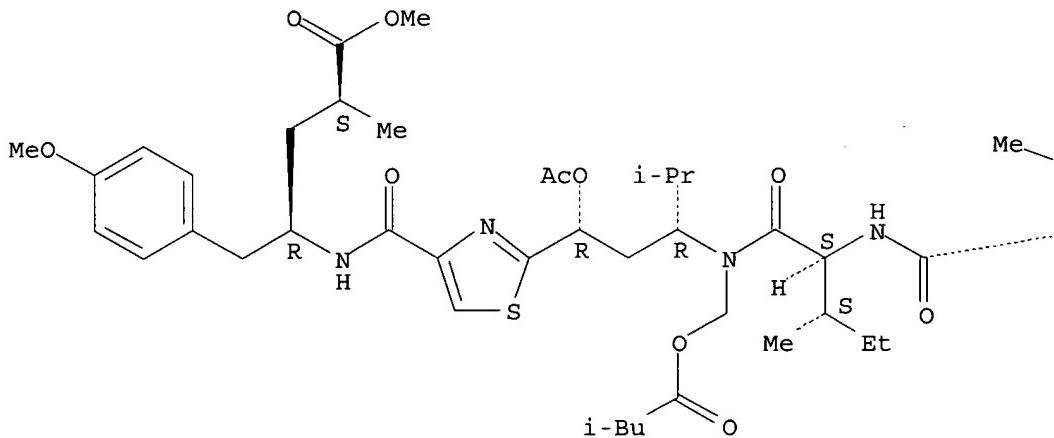
or base cleavage of the ester side chain)

RN 697236-88-7 HCPLUS

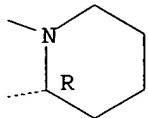
CN Benzenepentanoic acid,  $\gamma$ -[[[2-[(1R,3R)-1-(acetoxy)-4-methyl-3-[(2S,3S)-3-methyl-2-[[[(2R)-1-methyl-2-piperidinyl]carbonyl]amino]-1-oxopentyl][(3-methyl-1-oxobutoxy)methyl]amino]pentyl]-4-thiazolyl]carbonyl]amino]-4-methoxy- $\alpha$ -methyl-, methyl ester,  
 ( $\alpha$ S, $\gamma$ R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L6 ANSWER 4 OF 8 HCAPLUS COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 2004:216844 HCAPLUS  
 DOCUMENT NUMBER: 140:248261  
 TITLE: The gene cluster for enzymes of tubulysin biosynthesis of *Angiococcus disciformis* and its use in the manufacture of tubulysins for therapeutic use  
 INVENTOR(S): Hoefle, Gerhard; Mueller, Rolf; Sasse, Florenz; Sandmann, Axel; Bloecker, Helmut  
 PATENT ASSIGNEE(S): Gesellschaft fuer Biotechnologische Forschung m.b.H. (GBF), Germany  
 SOURCE: Ger. Offen., 56 pp.  
 CODEN: GWXXBX  
 DOCUMENT TYPE: Patent  
 LANGUAGE: German  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 10241152	A1	20040318	DE 2002-10241152	20020905
WO 2004022586	A2	20040318	WO 2003-EP9780	20030903
WO 2004022586	A3	20041111		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

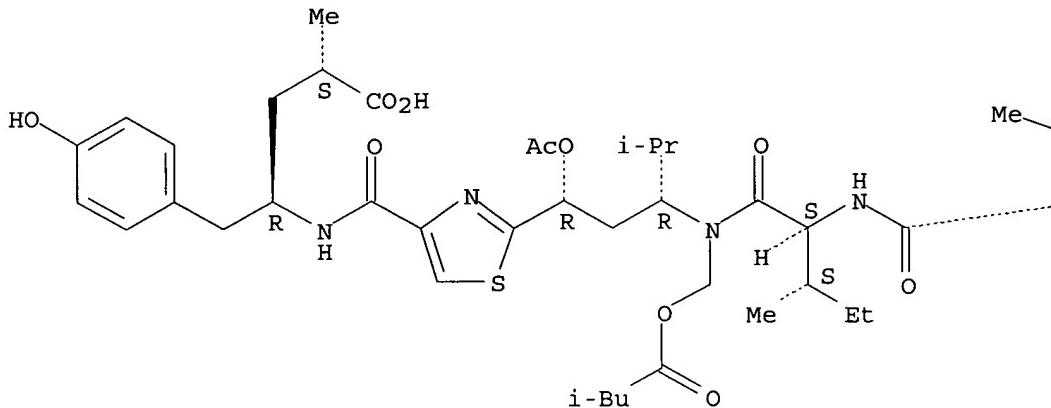
PRIORITY APPLN. INFO.: DE 2002-10241152 A 20020905  
 AB The gene cluster of *Angiococcus disciformis* encoding the enzymes of tubulysin biosynthesis is cloned and characterized. The genes may be expressed in other hosts for the manufacture of tubulysins. The genes were identified by transposon mutagenesis.

IT 205304-86-5DP, Tubulysin A, analogs, derivs. 205304-87-6DP, , Tubulysin B, analogs, derivs. 205304-88-7DP, Tubulysin C, analogs, derivs.  
 RL: BPN (Biosynthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (gene cluster for enzymes of tubulysin biosynthesis of *Angiococcus disciformis* and its use in manufacture of tubulysins for therapeutic use)  
 RN 205304-86-5 HCAPLUS

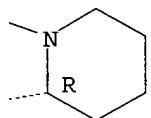
CN Benzenepentanoic acid,  $\gamma$ -[[[2-[(1R,3R)-1-(acetyloxy)-4-methyl-3-[(2S,3S)-3-methyl-2-[[[(2R)-1-methyl-2-piperidinyl]carbonyl]amino]-1-oxopentyl][(3-methyl-1-oxobutoxy)methyl]amino]pentyl]-4-thiazolyl]carbonyl]amino]-4-hydroxy- $\alpha$ -methyl-, ( $\alpha$ S, $\gamma$ R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

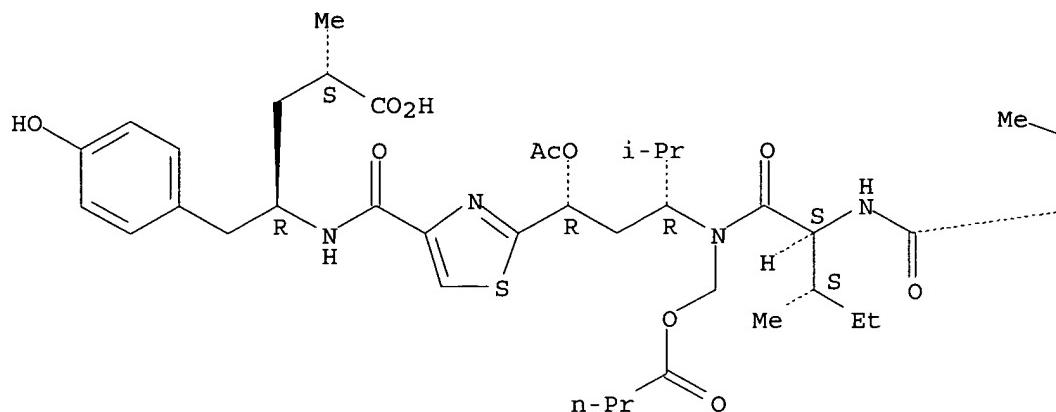


RN 205304-87-6 HCPLUS

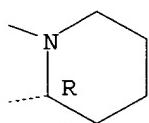
CN Benzenepentanoic acid,  $\gamma$ -[[[2-[(1R,3R)-1-(acetyloxy)-4-methyl-3-[(2S,3S)-3-methyl-2-[[[(2R)-1-methyl-2-piperidinyl]carbonyl]amino]-1-oxopentyl][(1-oxobutoxy)methyl]amino]pentyl]-4-thiazolyl]carbonyl]amino]-4-hydroxy- $\alpha$ -methyl-, ( $\alpha$ S, $\gamma$ R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

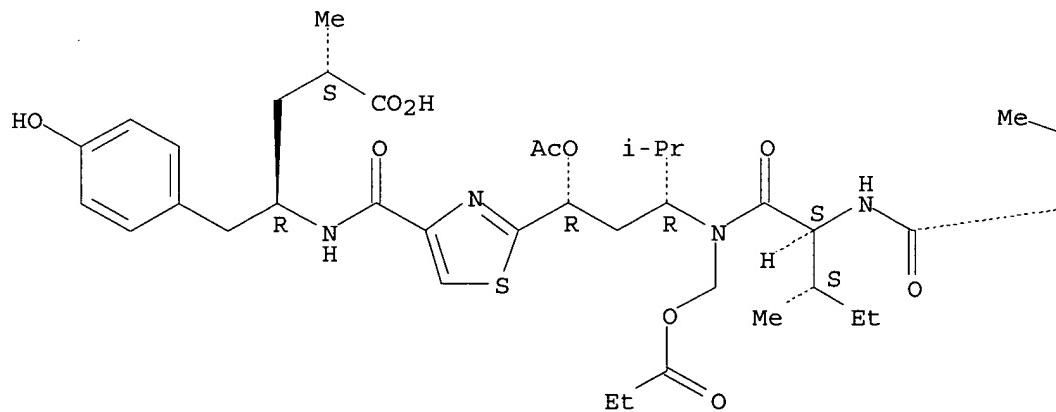


RN 205304-88-7 HCAPLUS

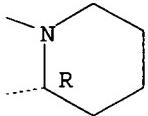
CN Benzenepentanoic acid,  $\gamma$ -[[[2-[(1R,3R)-1-(acetyloxy)-4-methyl-3-[(2S,3S)-3-methyl-2-[[[(2R)-1-methyl-2-piperidinyl]carbonyl]amino]-1-oxopentyl][(1-oxopropoxy)methyl]amino]pentyl]-4-thiazolyl]carbonyl]amino]-4-hydroxy- $\alpha$ -methyl-, ( $\alpha$ S, $\gamma$ R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L6 ANSWER 5 OF 8 HCAPLUS COPYRIGHT 2005 ACS on STN  
ACCESSION NUMBER: 2004:41504 HCAPLUS  
DOCUMENT NUMBER: 140:71010  
TITLE: Tubulysin conjugates with polymers or biomolecules,  
and use for the treatment of cancer  
INVENTOR(S): Doemling, Alexander; Weber, Lutz  
PATENT ASSIGNEE(S): Morphochem Aktiengellschaft fur Kombinatorische  
Chemie, Germany  
SOURCE: PCT Int. Appl., 21 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: German  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004005326	A2	20040115	WO 2003-EP7415	20030709
WO 2004005326	A3	20040219		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
DE 10230875	A1	20040122	DE 2002-10230875	20020709
DE 10305531	A1	20040819	DE 2003-10305531	20030211
EP 1521769	A2	20050413	EP 2003-762673	20030709
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK			
US 2005249740	A1	20051110	US 2005-520791	20050108
PRIORITY APPLN. INFO.:			DE 2002-10230875	A 20020709
			DE 2003-10305531	A 20030211
			WO 2003-EP7415	W 20030709

OTHER SOURCE(S): MARPAT 140:71010  
AB The invention discloses tubulysin conjugates (e.g. of tubulysin A) with polymer or biomols. (e.g. antibodies) and the use thereof in the treatment of cancers.  
IT 205304-86-5D, Tubulysin A, conjugates with polymers or biomols.

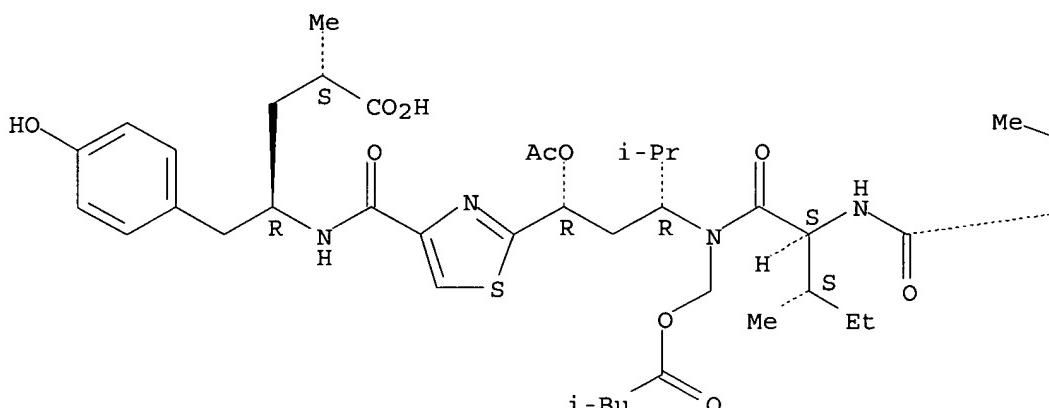
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (tubulysin conjugates with polymers or biomols., and use for treatment of cancer)

RN 205304-86-5 HCAPLUS

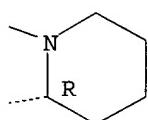
CN Benzenepentanoic acid,  $\gamma$ -[[[2-[(1R,3R)-1-(acetyloxy)-4-methyl-3-[(2S,3S)-3-methyl-2-[(2R)-1-methyl-2-piperidinyl]carbonyl]amino]-1-oxopentyl][(3-methyl-1-oxobutoxy)methyl]amino]pentyl]-4-thiazolyl]carbonylamino]-4-hydroxy- $\alpha$ -methyl-, ( $\alpha$ S, $\gamma$ R)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

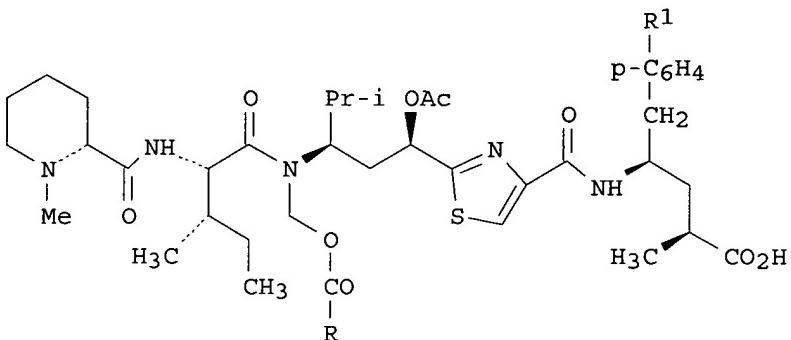


L6 ANSWER 6 OF 8 HCAPLUS COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 2001:794958 HCAPLUS  
 DOCUMENT NUMBER: 135:331296  
 TITLE: Preparation of stereospecific synthetic tubulysins and intermediates  
 INVENTOR(S): Hofle, Gerhard; Leibold, Thomas; Steinmetz, Heinrich  
 PATENT ASSIGNEE(S): Gesellschaft Fur Biotechnologische Forschung Mbh (Gbf), Germany  
 SOURCE: Ger. Offen., 22 pp.  
 CODEN: GWXXBX  
 DOCUMENT TYPE: Patent  
 LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

## PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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DE 10008089	A1	20011031	DE 2000-10008089	20000222
PRIORITY APPLN. INFO.:			DE 2000-10008089	20000222
OTHER SOURCE(S):	CASREACT 135:331296; MARPAT 135:331296			
GI				



AB Methods for the stereospecific synthesis of tubulysins (I; R = CH<sub>2</sub>CH<sub>3</sub>, (CH<sub>2</sub>)<sub>2</sub>CH(CH<sub>3</sub>)<sub>2</sub>; R<sub>1</sub> = H, OH) and their intermediates and stereoisomers were claimed (no data). The absolute stereochem. configuration of tubulysins was determined Steps in the preparation included reductive amination of (2S)-2-piperidine carboxylic acid and ring-opening of Boc-N-3-methyl-5-benzylpyrrolidin-2-one, which was prepared from BOC-Phe-OH.

IT 205304-86-5, Tubulysin A 205304-87-6, Tubulysin B  
205304-88-7, Tubulysin C

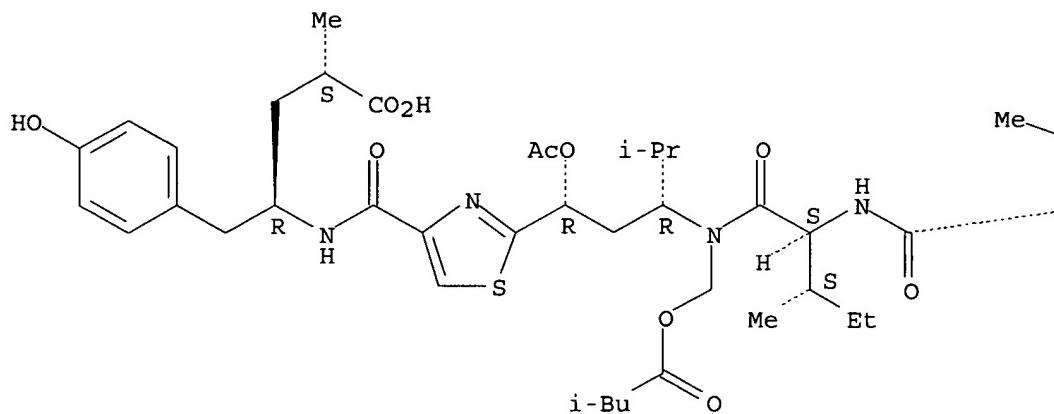
RL: NUU (Other use, unclassified); USES (Uses)  
(preparation of stereospecific synthetic tubulysins and intermediates)

RN 205304-86-5 HCPLUS

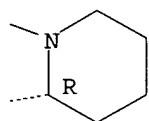
CN Benzenepentanoic acid,  $\gamma$ -[[2-[(1R,3R)-1-(acetyloxy)-4-methyl-3-[(2S,3S)-3-methyl-2-[(2R)-1-methyl-2-piperidinyl]carbonyl]amino]-1-oxopentyl][(3-methyl-1-oxobutoxy)methyl]amino]pentyl]-4-thiazolyl]carbonyl]amino]-4-hydroxy- $\alpha$ -methyl-, ( $\alpha$ S, $\gamma$ R)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

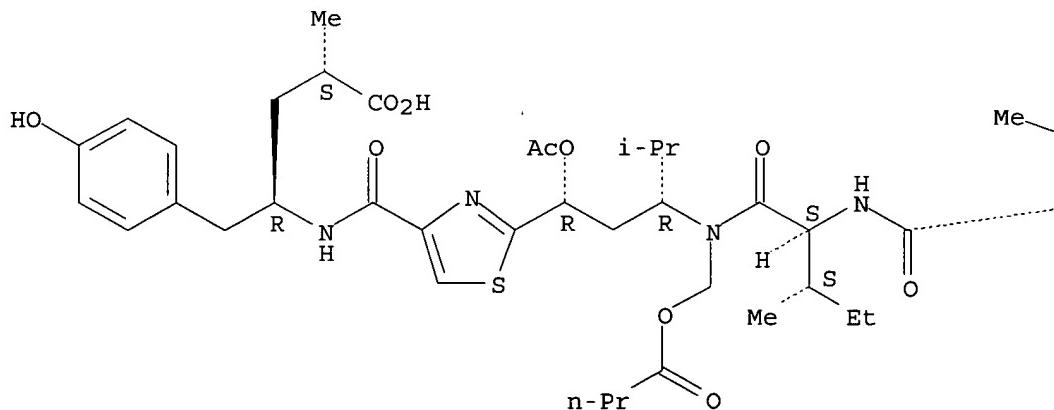


RN 205304-87-6 HCAPLUS

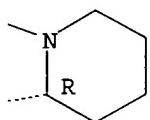
CN Benzenepentanoic acid,  $\gamma$ -[[[2-[(1R,3R)-1-(acetyloxy)-4-methyl-3-[(2S,3S)-3-methyl-2-[[[(2R)-1-methyl-2-piperidinyl]carbonyl]amino]-1-oxopentyl][(1-oxobutoxy)methyl]amino]pentyl]-4-thiazolyl]carbonyl]amino]-4-hydroxy- $\alpha$ -methyl-, ( $\alpha$ S, $\gamma$ R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



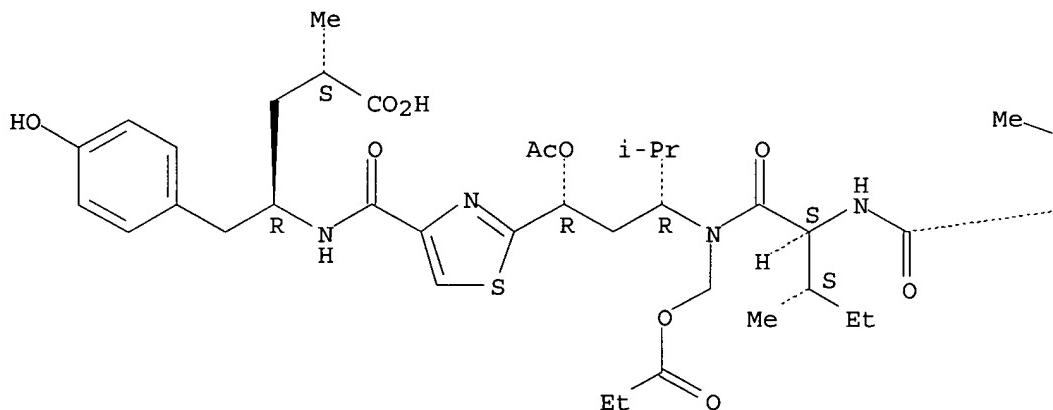
PAGE 1-B



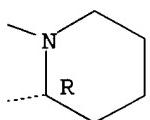
RN 205304-88-7 HCAPLUS  
CN Benzenepentanoic acid,  $\gamma$ -[[[2-[(1R,3R)-1-(acetyloxy)-4-methyl-3-  
[[[2(S,3S)-3-methyl-2-[[[(2R)-1-methyl-2-piperidinyl]carbonyl]amino]-1-  
oxopentyl][(1-oxopropoxy)methyl]amino]pentyl]-4-thiazolyl]carbonyl]amino]-  
4-hydroxy- $\alpha$ -methyl-, ( $\alpha$ S,  $\gamma$ R)- (9CI) (CA INDEX NAME)

## Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L6 ANSWER 7 OF 8 HCAPLUS COPYRIGHT 2005 ACS on STN  
ACCESSION NUMBER: 2000:702489 HCAPLUS

DOCUMENT NUMBER: 134:15006  
 TITLE: Tubulysins, new cytostatic peptides from myxobacteria acting on microtubuli. Production, isolation, physico-chemical and biological properties  
 AUTHOR(S): Sasse, Florenz; Steinmetz, Heinrich; Heil, Jurgen; Hofle, Gerhard; Reichenbach, Hans  
 CORPORATE SOURCE: GBF, Gesellschaft fur Biotechnologische Forschung mbH, Abteilung Naturstoffbiologie, Braunschweig, D-38124, Germany  
 SOURCE: Journal of Antibiotics (2000), 53(9), 879-885  
 CODEN: JANTAJ; ISSN: 0021-8820  
 PUBLISHER: Japan Antibiotics Research Association  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB New cytostatic compds., tubulysins, were isolated from the culture broth of strains of the myxobacteria Archangium gephyra and Angiococcus disciformis. The compds. are peptides partly consisting of unusual amino acids and are distantly related to the dolastatins. The tubulysins were not active against bacteria and only little against fungi, but showed high cytostatic activity against mammalian cell lines with IC<sub>50</sub> values in the picomolar range. An incubation with 50 ng/mL tubulysin A led to a complete disappearance of the microtubuli network of the cells within 24 h. The more active tubulysin D induced multipolar spindles; at 0.5 ng/mL all mitotic cells showed more than four spindle poles.

IT 205304-86-5P, Tubulysin A 205304-87-6P, Tubulysin B  
 RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BSU (Biological study, unclassified); PRP (Properties); PUR (Purification or recovery); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation)

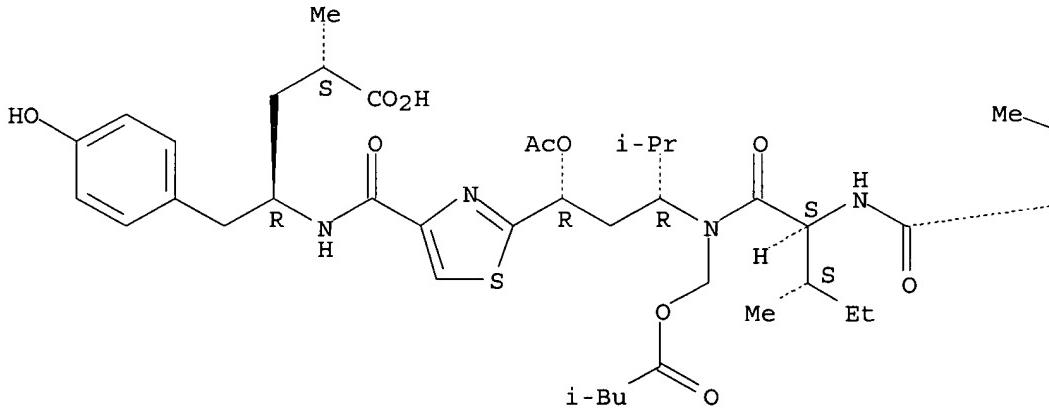
(tubulysins as new cytostatic peptides from myxobacteria acting on microtubuli)

RN 205304-86-5 HCPLUS

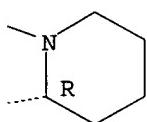
CN Benzenepentanoic acid,  $\gamma$ -[[[2-[(1R,3R)-1-(acetyloxy)-4-methyl-3-[(2S,3S)-3-methyl-2-[(2R)-1-methyl-2-piperidinyl]carbonyl]amino]-1-oxopentyl][(3-methyl-1-oxobutoxy)methyl]amino]pentyl]-4-thiazolyl]carbonyl]amino]-4-hydroxy- $\alpha$ -methyl-, ( $\alpha$ S, $\gamma$ R)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

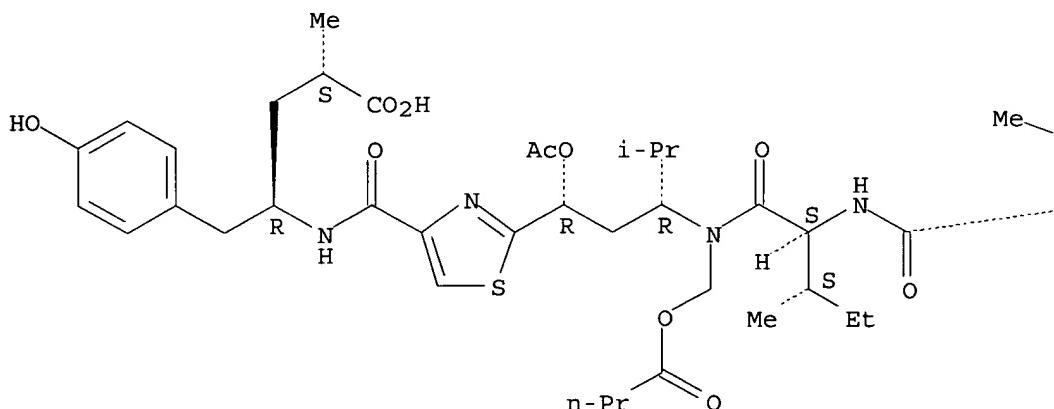


RN 205304-87-6 HCPLUS

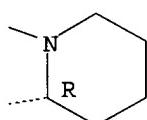
CN Benzenepentanoic acid,  $\gamma$ -[[[2-[(1R,3R)-1-(acetyloxy)-4-methyl-3-[(2S,3S)-3-methyl-2-[[[(2R)-1-methyl-2-piperidinyl]carbonyl]amino]-1-oxopentyl][(1-oxobutoxy)methyl]amino]pentyl]-4-thiazolyl]carbonyl]amino]-4-hydroxy- $\alpha$ -methyl-, ( $\alpha$ S, $\gamma$ R) - (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



REFERENCE COUNT:

11

THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 8 OF 8 HCPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1998:208578 HCAPLUS  
 DOCUMENT NUMBER: 128:256473  
 TITLE: Antimycotic and cytostatic compounds manufacture with Archangium  
 INVENTOR(S): Reichenbach, Hans; Hoefle, Gerhard; Sasse, Florenz;  
 Steinmetz, Heinrich  
 PATENT ASSIGNEE(S): Gesellschaft fuer Biotechnologische Forschung m.b.H.  
 (GBF), Germany  
 SOURCE: Ger. Offen., 16 pp.  
 CODEN: GWXXBX  
 DOCUMENT TYPE: Patent  
 LANGUAGE: German  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 19638870	A1	19980326	DE 1996-19638870	19960923
WO 9813375	A1	19980402	WO 1997-EP5095	19970917
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9745550	A1	19980417	AU 1997-45550	19970917
PRIORITY APPLN. INFO.:			DE 1996-19638870	A 19960923
			WO 1997-EP5095	W 19970917

GI

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB Tubulysin A (I), B (II), and C (III) are manufactured by culturing *A. gephyra* isolated from a compost sample. Shake-culture of *A. gephyra* in a medium of single-cell protein preparation (Probion), yeast extract, glucose, etc., and chromatog. isolation of I, II, and III were shown. The physicochem. characteristics for these antimycotic and cytotoxic compds. were given. Also given was inhibition of fungus, and human and animal neoplastic cell lines with these Tubulysins.

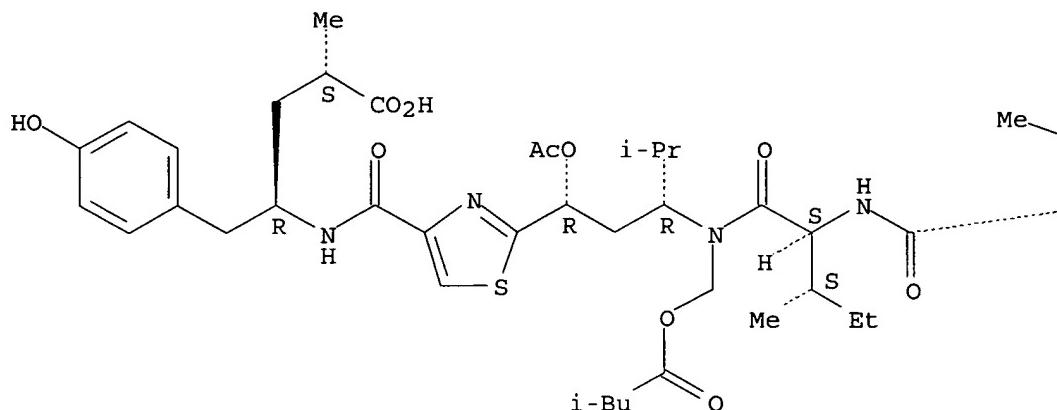
IT 205304-86-5P, Tubulysin A 205304-87-6P, Tubulysin B  
 205304-88-7P, Tubulysin C  
 RL: BPN (Biosynthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (antimycotic and cytostatic compds. manufacture with Archangium)

RN 205304-86-5 HCAPLUS

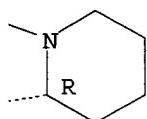
CN Benzenepentanoic acid,  $\gamma$ -[[[2-[(1R,3R)-1-(acetoxy)-4-methyl-3-[(2S,3S)-3-methyl-2-[[[(2R)-1-methyl-2-piperidinyl]carbonyl]amino]-1-oxopentyl][(3-methyl-1-oxobutoxy)methyl]amino]pentyl]-4-thiazolyl]carbonyl]amino]-4-hydroxy- $\alpha$ -methyl-, ( $\alpha$ S, $\gamma$ R)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

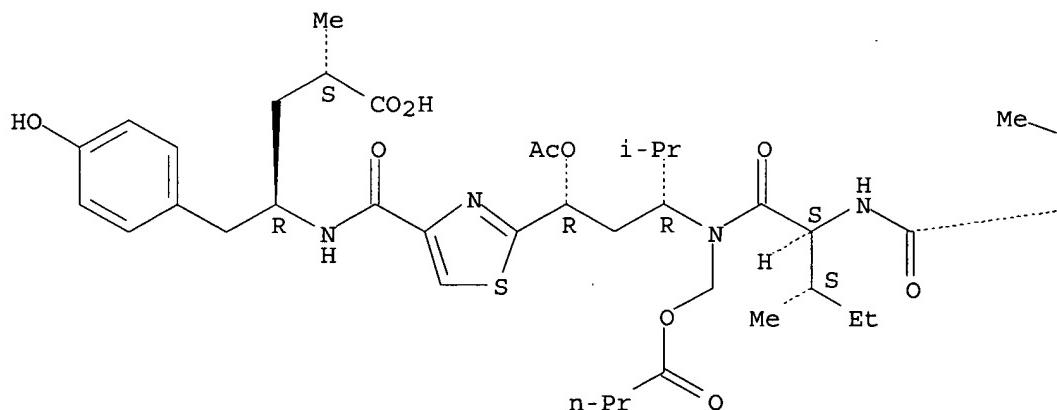


RN 205304-87-6 HCAPLUS

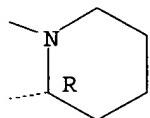
CN Benzenepentanoic acid,  $\gamma$ -[[[2-[(1R,3R)-1-(acetyloxy)-4-methyl-3-[(2S,3S)-3-methyl-2-[[[(2R)-1-methyl-2-piperidinyl]carbonyl]amino]-1-oxopentyl][(1-oxobutoxy)methyl]amino]pentyl]-4-thiazolyl]carbonyl]amino]-4-hydroxy- $\alpha$ -methyl-, ( $\alpha$ S, $\gamma$ R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



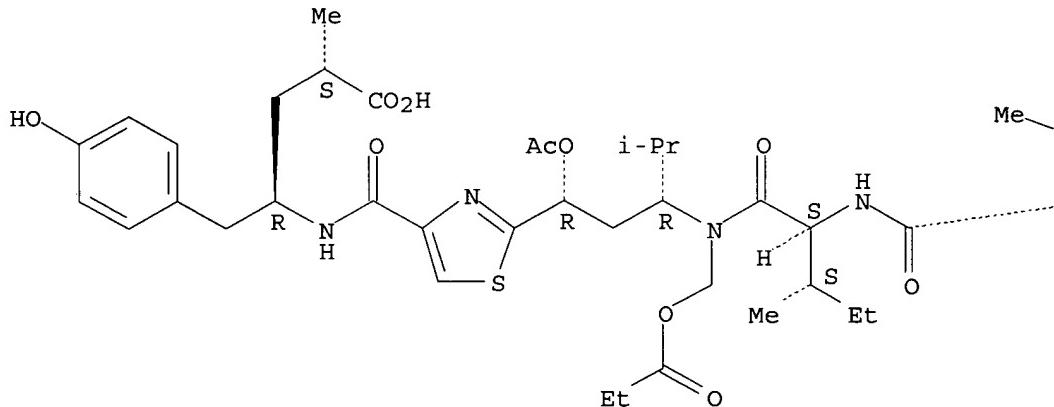
PAGE 1-B



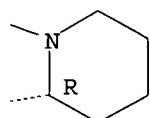
RN 205304-88-7 HCAPLUS  
 CN Benzenepentanoic acid,  $\gamma$ -[[[2-[(1R,3R)-1-(acetyloxy)-4-methyl-3-[(2S,3S)-3-methyl-2-[(2R)-1-methyl-2-piperidinyl]carbonyl]amino]-1-oxopentyl][(1-oxopropoxy)methyl]amino]pentyl]-4-thiazolyl]carbonyl]amino]-4-hydroxy- $\alpha$ -methyl-, ( $\alpha$ S, $\gamma$ R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



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'BEISTEIN' IS NOT A VALID FILE NAME  
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FILE LAST UPDATED ON OCTOBER 10, 2005

FILE COVERS 1771 TO 2005.

\*\*\* FILE CONTAINS 9,363,954 SUBSTANCES \*\*\*

>>> PLEASE NOTE: Reaction Data and substance data are stored in separate documents and can not be searched together in one query. Reaction data for BEILSTEIN compounds may be displayed immediately with the display codes PRE (preparations) and REA (reactions). A substance answer set retrieved after the search for a chemical name, a compounds with available reaction information by combining with PRE/FA, REA/FA or more generally with RX/FA. The BEILSTEIN Registry Number (BRN) is the link between a BEILSTEIN compound and belonging reactions. For more detailed reaction searches BRNs can be searched as reaction partner BRNs Reactant BRN (RX.RBRN) or Product BRN (RX.PBRN). <<<

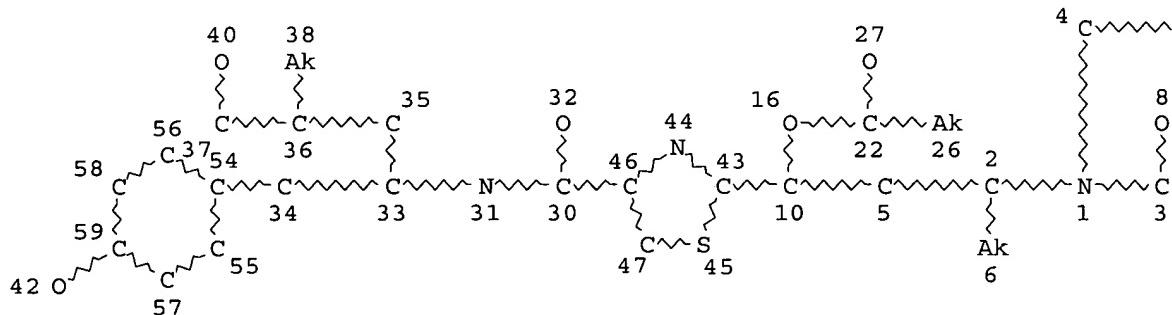
>>> FOR SEARCHING PREPARATIONS SEE HELP PRE <<<

\*\*\*\*\*  
\* PLEASE NOTE THAT THERE ARE NO FORMATS FREE OF COST. \*  
\* SET NOTICE FEATURE: THE COST ESTIMATES CALCULATED FOR SET NOTICE \*  
\* ARE BASED ON THE HIGHEST PRICE CATEGORY. THEREFORE; THESE \*  
\* ESTIMATES MAY NOT REFLECT THE ACTUAL COSTS. \*  
\* FOR PRICE INFORMATION SEE HELP COST \*  
\*\*\*\*\*

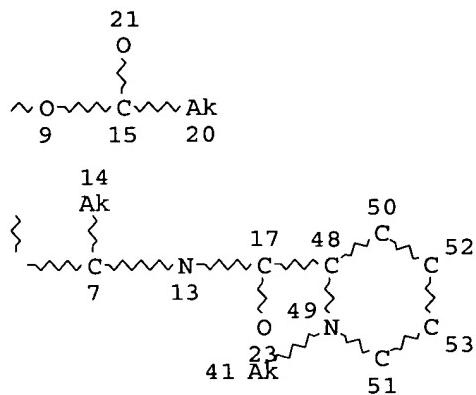
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\* PATENT NUMBERS (PN) AND BABS ACCESSION NUMBERS (BABSAN) CAN NOW BE  
SEARCHED, SELECTED AND TRANSFERRED.  
\* NEW DISPLAY FORMATS ALLREF, ALLP AND BABSAN SHOW ALL REFERENCES,  
ALL PATENT REFERENCES, OR ALL BABS ACCESSION NUMBERS FOR A  
COMPOUND AT A GLANCE.

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L3 STR



Page 1-A



Page 1-B

NODE ATTRIBUTES:

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DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

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STEREO ATTRIBUTES: NONE

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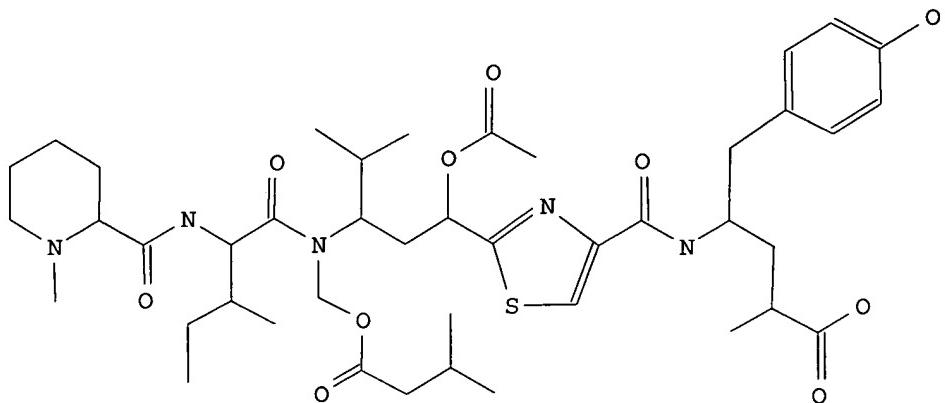
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2 ANSWERS

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L9 ANSWER 1 OF 2 BEILSTEIN COPYRIGHT 2005 BEILSTEIN MDL on STN

Beilstein Records (BRN) :	8749454
Chemical Name (CN) :	tubulysin A
Autonom Name (AUN) :	4-(<2-<1-acetoxy-4-methyl-3-((3-methyl-butryloxyethyl)-<3-methyl-2-<(1-methyl-piperidine-2-carbonyl)-amino>-pentanoyl>-amino)-pentyl>-thiazole-4-carbonyl>-amino)-5-(4-hydroxy-phenyl)-2-methyl-pentanoic acid
Molec. Formula (MF) :	C43 H65 N5 O10 S
Molecular Weight (MW) :	844.07
Lawson Number (LN) :	31708, 26276, 16221, 3409, 2817, 1183, 1155, 689
Compound Type (CTYPE) :	heterocyclic
Constitution ID (CONSID) :	7409616
Tautomer ID (TAUTID) :	8237429
Entry Date (DED) :	2001/04/26
Update Date (DUPD) :	2001/04/26



## Field Availability:

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AUN	Autonomname	1
MF	Molecular Formula	1
FW	Formular Weight	1
LN	Lawson Number	8
CTYPE	Compound Type	1
CONSID	Constitution ID	1
TAUTID	Tautomer ID	1
DED	Entry Date	1
DUPD	Update Date	1
INP	Isolation from Natural Product	2
IR	Infrared Spectrum	1
PHARM	Pharmacological Data	18
UVS	UV and Visible Spectrum	1

## All References:

ALLREF

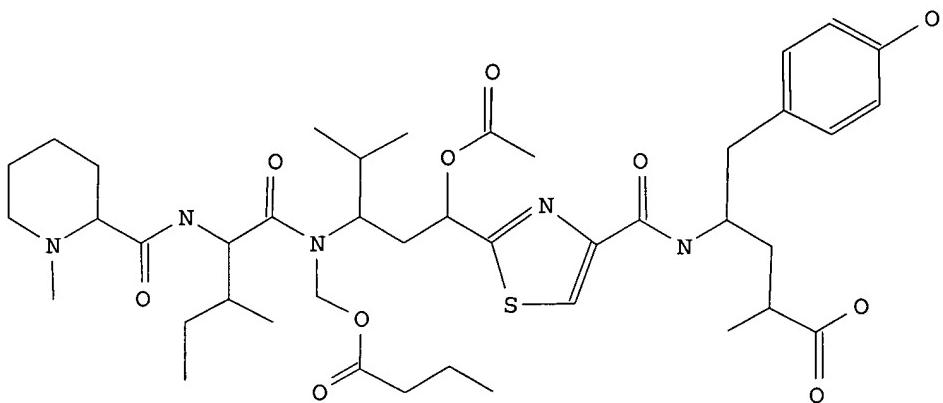
1. Sasse, Florenz; Steinmetz, Heinrich; Heil, Juergen; Hoelfe, Gerhard; Reichenbach, Hans, J.Antibiot., CODEN: JANTAJ, 53(9), <2000>, 879 - 885; BABS-6265536

=&gt; d 19 ide allref 2

L9 ANSWER 2 OF 2 BEILSTEIN COPYRIGHT 2005 BEILSTEIN MDL on STN

Beilstein Records (BRN) : 8749373  
 Chemical Name (CN) : tubulysin B  
 Autonom Name (AUN) : 4-(<2-<1-acetoxy-3- (butyryloxymethyl-<3-methyl-2-<(1-methyl-piperidine-2-carbonyl)-amino>-pentanoyl>-amino) -4-methyl-pentyl>-thiazole-4-carbonyl>-amino) -5-(4-hydroxy-phenyl)-2-methyl-pentanoic acid

Molec. Formula (MF) : C42 H63 N5 O10 S  
 Molecular Weight (MW) : 830.05  
 Lawson Number (LN) : 31708, 26276, 16221, 3409, 2817, 1173,  
                       1155, 689  
 Compound Type (CTYPE) : heterocyclic  
 Constitution ID (CONSID) : 7409548  
 Tautomer ID (TAUTID) : 8237425  
 Entry Date (DED) : 2001/04/26  
 Update Date (DUPD) : 2001/04/26



## Field Availability:

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CN	Chemical Name	1
AUN	Autonomname	1
MF	Molecular Formula	1
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DED	Entry Date	1
DUPD	Update Date	1
INP	Isolation from Natural Product	2
PHARM	Pharmacological Data	16
UVS	UV and Visible Spectrum	1

## All References:

ALLREF

1. Sasse, Florenz; Steinmetz, Heinrich; Heil, Juergen; Hoelfe, Gerhard; Reichenbach, Hans, J.Antibiot., CODEN: JANTAJ, 53(9), <2000>, 879 - 885; BABS-6265536

=&gt; file marpat

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FILE CONTENT: 1988-PRESENT (VOL 143 ISS 24) (20051211/ED)

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 (COVERAGE TO THESE DATES IS NOT COMPLETE):

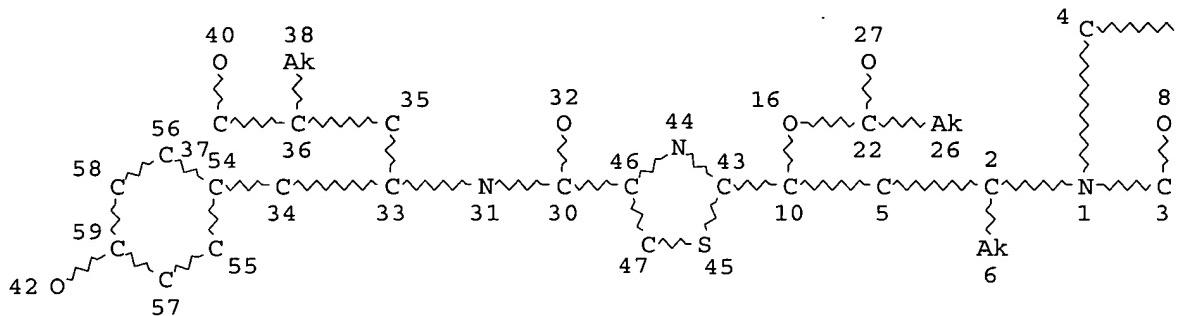
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 EP 1577935 21 SEP 2005  
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 WO 2005097137 20 OCT 2005

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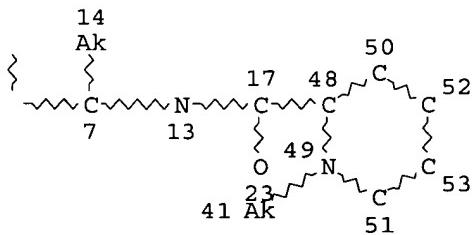
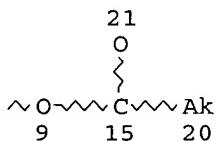
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MARPATpreviews will be removed from STN on December 31, 2005.

=> d que stat 113  
 L3 STR



Page 1-A



Page 1-B

NODE ATTRIBUTES:

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DEFAULT ECLEVEL IS LIMITED

## GRAPH ATTRIBUTES:

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## STEREO ATTRIBUTES: NONE

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L6 8 SEA FILE=HCAPLUS ABB=ON PLU=ON L5  
L12 3 SEA FILE=MARPAT SSS FUL L3  
L13 0 SEA FILE=MARPAT ABB=ON PLU=ON L12 NOT L6